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15, 16, 17 October 1956

Official Publication
AMERICAN COLLEGE
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1. Watt, B. K., and Merrill, A. L.: Composition of Foods—Raw, Processed, Prepared, Washington, D. C., United States Department of Agriculture, Agricultural Handbook No. 8, 1950.
2. Sherman, H. C.: Chemistry of Food and Nutrition, ed. 8, New York, The Macmillan Company, 1952, p. 598.
3. Facts on Oats: Report by the Research Laboratories of The Quaker Oats Company, 1955.
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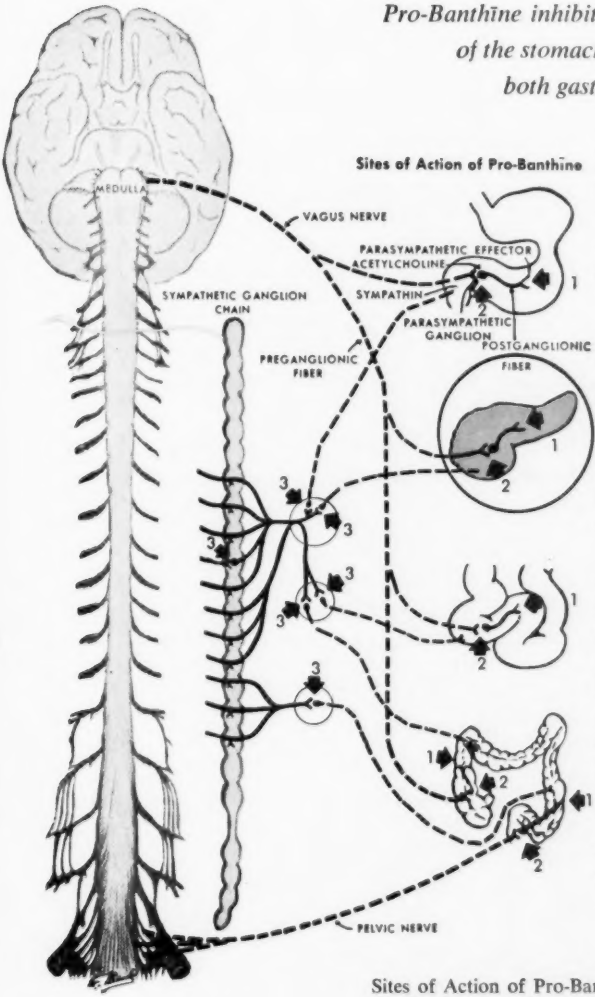

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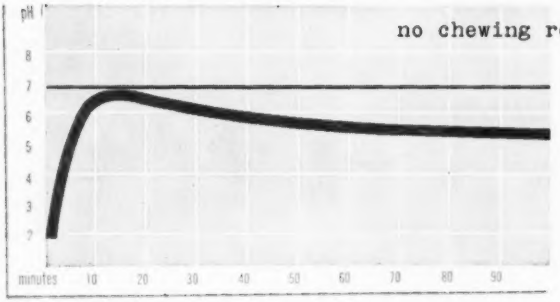

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VOL. 26, No. 1 JULY, 1956

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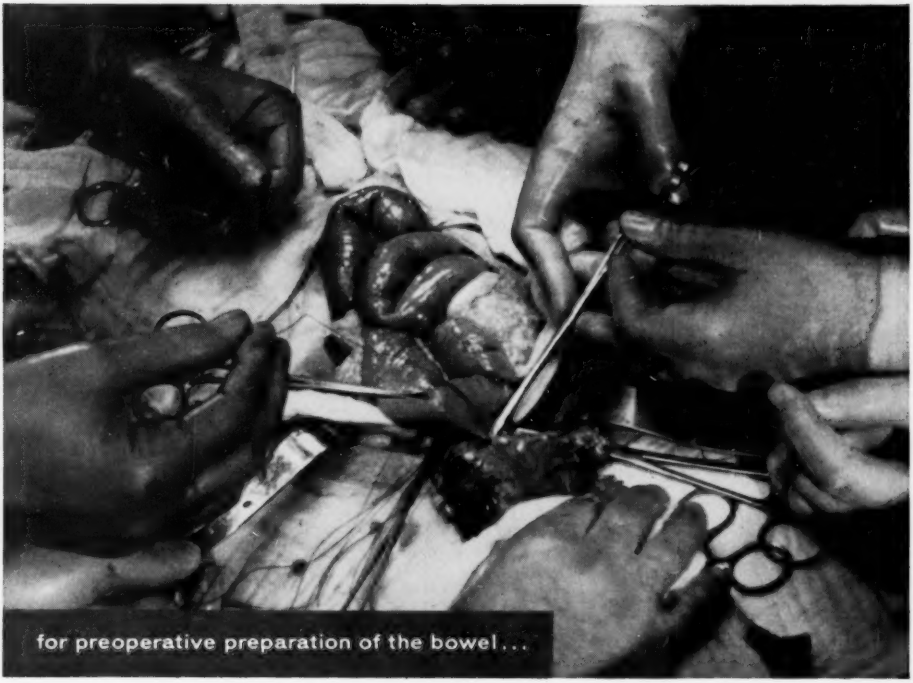

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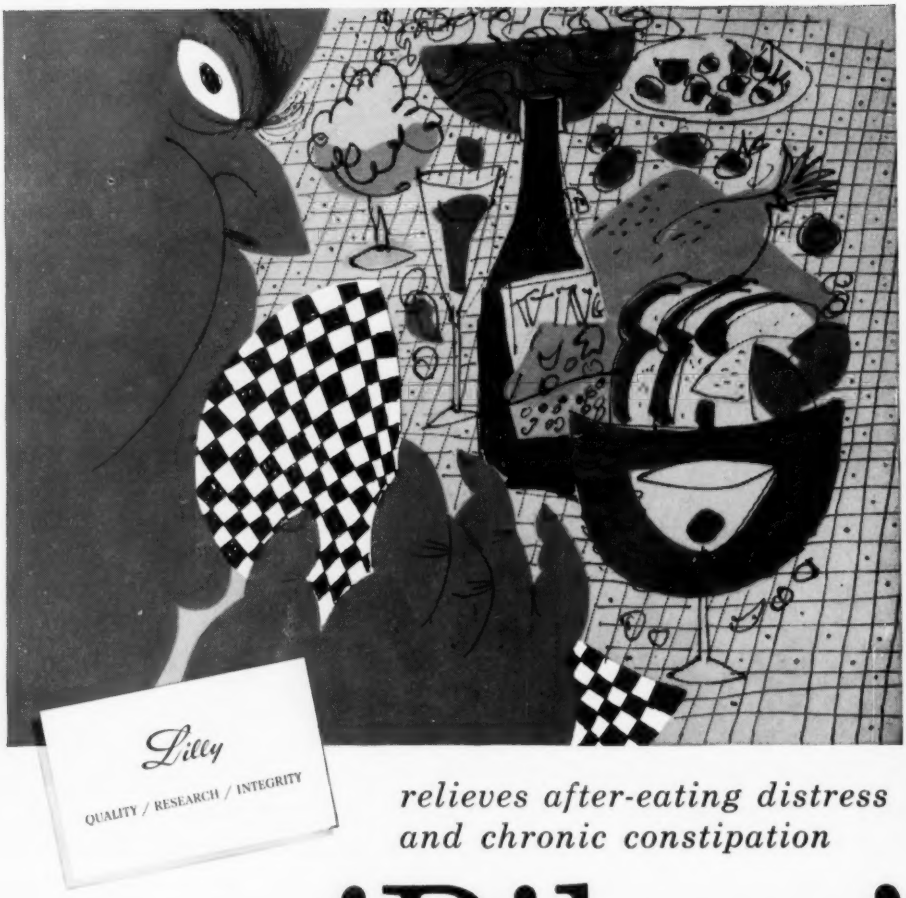

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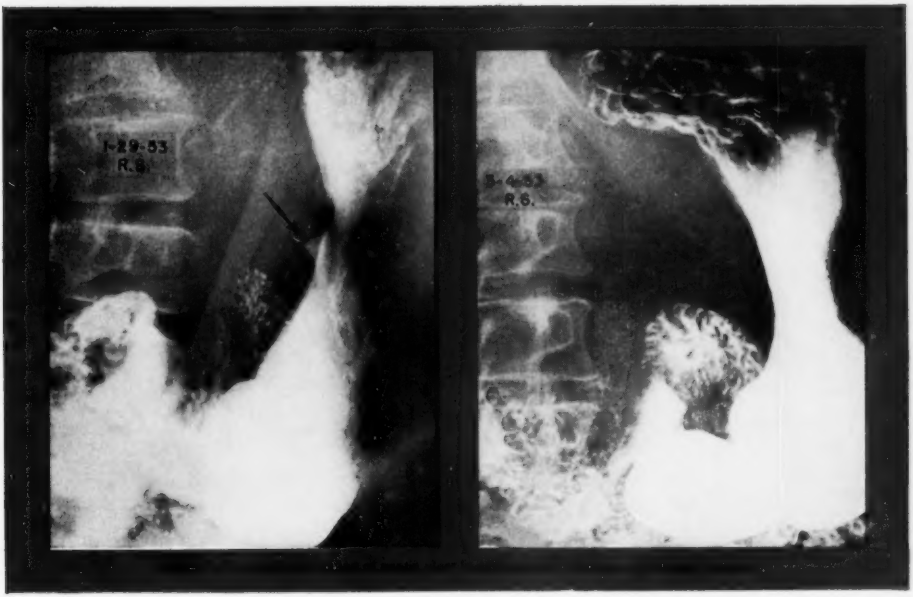

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1. Barrett, W. E., Rutledge, R., Plummer, A. J., and Yonkman, F. F.: J. Pharmacol. & Exper. Therap. *108*:305 (July) 1953. 2. Rogers, M. P., and Gray, C. L.: Am. J. Digest. Dis. *19*:180 (June) 1952.

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SOME SURGICAL PROBLEMS OF THE ORAL CAVITY AND RELATED STRUCTURES*

BERNARD G. SARNAT, M.D.†
Beverly Hills, Calif.

INTRODUCTION

The material which follows will in no way attempt to be a detailed description of the diagnosis and treatment of surgical conditions of the mouth. Surgery of the oral cavity and related structures is essentially no different from surgery elsewhere in the body. The same principles of general surgery must be followed and not violated. Frequently the principles of plastic surgery must be employed in the treatment of oral surgical problems. Plastic surgery, whether in the mouth or elsewhere requires accurate planning, precision and meticulous attention to details.

Surgery in the mouth is complicated by the relatively small size of the field, difficulty in approach and exposure and the need for suction of saliva and blood to maintain both visibility and an open airway. When general anesthesia is necessary, oral or nasal endotracheal intubation is used, in order to remove the anesthetist, as well as his apparatus, from the field.

Generally wounds of the oral cavity heal well. The fact that it is a warm, dark, moist cavity which houses a varied bacterial flora and which is subject to the trauma and motion of mastication does not usually interfere with healing. The routine use of chemotherapeutic or antibiotic agents is neither recommended nor necessary. The diet, depending upon the particular surgical procedure, may vary from a clear liquid to a soft, non-chewy consistency. It is important that it be made as appetizing as possible and include an adequate number of calories and essential foodstuffs. The use of an asepto syringe with

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†Formerly Attending Staffs, Michael Reese and Woodlawn Hospitals. Professor and Head, Department of Oral and Maxillofacial Surgery, and Clinical Assistant Professor, Division of Plastic Surgery, Department of Surgery, Colleges of Dentistry and Medicine, University of Illinois, Chicago, Ill.

attached rubber tubing (approximately 6 inches in length) inserted in the oral pharynx may facilitate the dietary intake. Oral hygiene is essential. Hot normal saline (500 c.c.) used as an irrigation or mouth wash will mechanically cleanse the mouth and reduce the inflammation and pain. This can be done several times a day beginning about 24 hours postoperatively. The addition of 50 to 100 c.c. of 3 per cent hydrogen peroxide to the solution or on cotton applicators will facilitate the cleansing action. A soft small tooth brush and dentrifice should be used when possible. This can be followed with a flavored

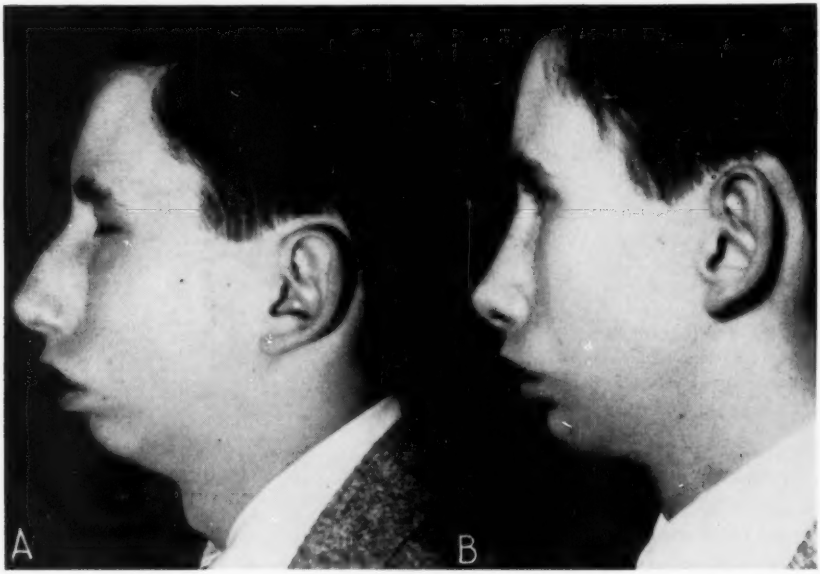

Fig. 1—Underdevelopment of mandible and bilateral facial palsy in a patient with history of possible birth injury to mandibular condyles and facial nerves. A. Preoperative. B. Postoperative, after autogenous cartilage rib transplant to chin and rhinoplasty. After the upper anterior teeth have been moved posteriorly by orthodontia, a second piece of cartilage (implanted subcutaneously in the abdominal wall) may be added to the chin, if necessary.

mouth wash. The vermilion border of the lips can be anointed with mineral oil or cold cream in order to keep them soft and free from drying, crusting and cracking.

Diagnosis and Treatment

It is difficult to develop an entirely satisfactory classification of surgical conditions of the oral cavity and associated structures. The following classification (Table I), although not all-inclusive and at times arbitrary, mentions the

more common and important conditions, only a few of which will be briefly discussed. Although certain lesions could be listed several times because they appropriately belong to more than one group, they are generally listed only once. The reader is referred to textbooks dealing with oral, maxillofacial and plastic surgery for a more complete discussion[1].

Developmental lesions:—Although abnormalities of the mouth found at birth may be of local origin, it is important to remember that they may be related to systemic conditions. Some of the more common developmental conditions of the jaws are: 1. under- and overdevelopment and 2. cleft palate. Any child with a malformation of the oral cavity should be examined for other anomalies such as imperforate anus, *spina bifida*, hydrocephalus, syndactylism, etc.

The most important growth center of the mandible is the condyle[2]. Total or partial absence of the condylar growth center is associated with anomalies of the temporomandibular joint and ear. The mandible and face on the affected side are smaller. In order to lessen the deformity, the mandible has been positioned anteriorly by means of a sliding osteotomy of the body or ramus. Usually, however, a masking operation by means of implanted cartilage proves to be a more satisfactory procedure (Fig. 1). Increased activity of the condylar growth center, the cause of which is unknown (except in cases of hyperpituitarism) results in a larger than normal mandible. Usually both sides are involved. Surgical treatment is directed toward retropositioning of the mandible by means of a subcondylar or transramus osteotomy or ostectomy of the body.

In some patients with an underdeveloped maxilla a cleft palate is sometimes found. The cleft palate, which may be either unilateral or bilateral and either partial or complete, is frequently associated with a cleft of the upper lip (Fig. 2). Several different surgical procedures have been used to close the cleft of the lip and palate. There is considerable lack of agreement, however, as to when a cleft palate should be closed surgically and, if so, at what time and by what method.

Inflammatory lesions include:—Dental infections and related conditions:—Oral and facial abscesses are usually secondary to infections of the teeth and jaws. In the mouth pathogenic organisms are introduced to the jaws through the separation between the gingiva and the teeth (lateral abscess) or as a result of dental caries with infection and death of the pulp with a spread to the root end region (periapical abscess and osteomyelitis). The direction of spread (intraoral or extraoral) of the abscess will depend upon the particular location in the upper or lower jaw of the tooth roots and their relationship to muscle and fascial planes. The acute phase may extend into a chronic one characterized by formation of a periapical dental granuloma, abscess or chronic draining sinuses opening into the mouth or on to the face or neck. A patient with a chronic sinus (draining or not) of the skin of the face or neck should be examined to see whether a dental infection is the possible source.

TABLE I

A Classification of Oral Lesions

I. Developmental lesions
  A. Soft tissue
    1. Labial pits
    2. Cleft lip
    3. Macroglossia
    4. Frena
    5. Median rhomboid glossitis
    6. Lingual thyroid
    7. Thyroglossal duct cyst
    8. Ectopic sebaceous glands (Fordyce's spots)
  B. Jaws
    1. Under- and overdevelopment
    2. Cleft palate
    3. *Torus mandibularis* and *palatinus*

II. Inflammatory lesions
  A. Aphthous stomatitis
  B. Vincent's
  C. Noma
  D. Moniliasis
  E. Pyogenic granuloma
  F. Dental infections and related conditions
  G. Syphilis
  H. Actinomycosis
  I. Blastomycosis
  J. Histoplasmosis
  K. Tuberculosis
  L. Eosinophilic granuloma
  M. Sarcoidosis
  N. Sialadenitis

III. Traumatic lesions
  A. Acute
    1. Bone (fractures)
    2. Soft tissue
      a. Chemical (lye, lysol)
      b. Physical (lacerations, bites, thermal, radiation, and electrical burns)
  B. Chronic
    1. Soft tissue
      a. Chemical
      b. Physical (denture irritation, cheek bites)
    2. Bone
      a. Chemical (heavy metal)
      b. Physical (radiation)

IV. Tumor and tumor-like lesions
  A. Benign
    1. Soft tissue
      a. Cystic
        1) Mucous gland
        2) Ranula
        3) Nasoalveolar
      b. Solid
        1) Epithelial
          (a) Adenomas

(b) Pleomorphic adenoma (salivary gland mixed tumor)
(c) Nevus
(d) Papilloma
2) Nonepithelial
(a) Gingival enlargements
(1) Pregnancy
(2) Dilantin sodium
(3) Fibromatosis
(4) "Epulis"
(b) Fibroma
(c) Hemangioma
(d) Lymphangioma
(e) Lipoma
(f) Myxoma
(g) Neuroma
(h) Neurofibroma
3) Composite tumors
(a) Dermoid
(b) Teratoma
2. Bone (Central lesions)
a. Nondental in origin
1) Solid
(a) Fibroma
(b) Ossifying fibroma
(c) Osteoma
(d) Chondroma
(e) Giant cell node (local)
2) Cystic
(a) Incisive canal
(b) Median anterior maxillary
(c) Traumatic
b. Dental in origin
1) Solid
(a) Granuloma
(b) Odontoma
(c) Cementoma
(d) Periapical ossifying fibroma
(e) Ameloblastoma
2) Cystic
(a) Follicular
(b) Dentigerous
(c) Dental eruption cyst
(d) Ameloblastoma
(e) Radicular

B. Precancerous
1. Leukoplakia
2. Papilloma
3. Chronic ulcer
4. Chronic fissure

C. Malignant
1. Epithelial in origin (carcinoma)
a. Primary
1) Bowen's disease (carcinoma *in situ*)
2) Epidermoid carcinoma
3) Adenocarcinoma
4) Melanoma
b. Metastatic to jaws (prostate, breast, thyroid, ovary, kidney, lung, and rectum)

2. Nonepithelial in origin (sarcoma)
   a. Primary
      1) Fibrosarcoma
      2) Osteogenic sarcoma
      3) Ewing's tumor
      4) Chondrosarcoma
      5) Lymphosarcoma
      6) Myxosarcoma
   b. Metastatic to jaws
   c. Generalized
      1) Hodgkin's disease
      2) Leukemia
      3) Multiple myeloma

V. Endocrine and metabolic lesions
   A. Diabetes mellitus
   B. Hyperparathyroidism
   C. Pregnancy
   D. Vitamin deficiency
   E. Dilantin sodium
   F. Blood dyscrasias
   G. Lipoid dystrophies
   H. Paget's bone disease

VI. Dermatologic lesions
   A. *Lichen planus*
   B. Psoriasis
   C. *Lupus erythematosus*
   D. Pemphigus

VII. Allergic conditions

Osteomyelitis of the jaws is more often a result of local rather than systemic factors. The acute type is frequently secondary to infection of the dental pulp, but may also result from a retained dental root or fractures of the jaws. Although the acute type may become chronic, the latter is more commonly associated with secondarily infected cysts, heavy metal poisoning, various radiations, tuberculosis, syphilis, and actinomycosis. In chronic osteomyelitis there may be acute recurrent exacerbations. In the presence of teeth the periodontal structures serve as a pathway for the spread of infection. Seldom does osteomyelitis begin in the edentulous jaw.

In the acute stage of osteomyelitis, roentgenographic evidence may not be found during the first few weeks. In the chronic stages, however, destruction of bone may be seen in the roentgenogram. Malignancies of the bone also show evidence of destruction on the roentgenogram and should be considered in the differential diagnosis.

Treatment should be directed toward prevention and elimination of the etiologic agent. Proper dental care will decrease the frequency of pulpitis and periapical infection. Patients who are administered heavy metals or radiation, particularly in the mouth, should receive excellent oral care, including removal of teeth with pathologic changes which might give rise to complications. The

judicious prophylactic and therapeutic use of the indicated antibiotics or chemotherapeutic agents has been of inestimable value. There is no substitute, however, for surgical treatment. Local treatment includes 1. drainage, 2. removal of nonvital tissue and 3. subsequent plastic surgical procedures for reconstruction of the residual deformity. Abscesses must be incised and drained. Planning of the incision is important as pertains to adequate drainage, avoidance of important structures and an inconspicuous scar, especially around the face. The underlying tissues are spread by blunt dissection to the source of the infection, which is usually at the bone. Infected roots, sequestra and foreign bodies should be removed. A small rubber drain is inserted. Sometimes

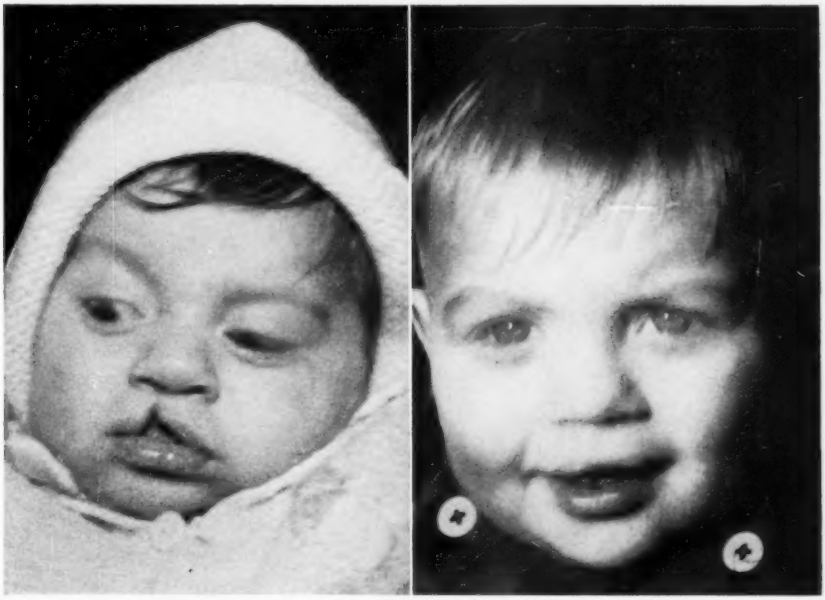

Fig. 2—Cleft lip and cleft palate. The cleft of the lip is corrected surgically usually within the first few weeks after birth whereas the cleft palate is not ordinarily repaired until some time after the first year.

a deep-seated abscess with overlying indurated tissue will not be fluctuant. Nevertheless, incision and drainage is indicated.

Sialadenitis:—Suppuration of the salivary glands may be acute or chronic. The acute type is found most frequently in the parotid gland of debilitated patients. The onset is sudden, the gland becomes swollen and hard, and pressure on the facial nerve may cause a palsy. Fluctuation may not be obtained because of the toughness of the parotid fascia. The papilla of the opening of the parotid duct is swollen and red, and a thick purulent discharge can be noted. To

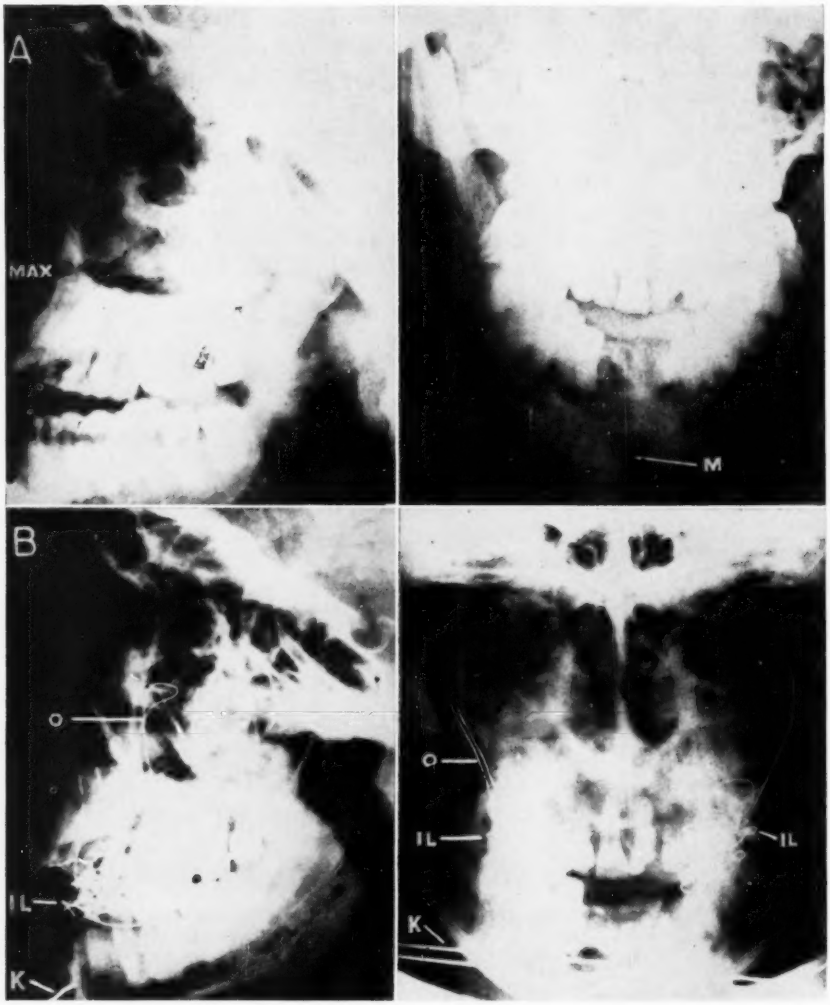

Fig. 3—Preoperative (A) and postoperative (B) x-ray pictures illustrating a combination of several fractures and several methods of treatment. This patient had multiple facial fractures including alveolar, mandibular (M), and complete transverse maxillary (MAX). Note malocclusion in (A). In this instance it was necessary to extract the loose teeth, reduce the fracture of the mandible, and by means of Kirschner wires (K) driven through the body of the mandible the fracture was fixed. Then by means of Ivy loops (IL) the mandible was wired to the maxilla. Next holes were drilled in each orbital floor and wires (O) passed through the holes, along the maxilla, through the buccal mucosa, into the mouth. These wires were then attached to the Ivy loops. This fixed the maxillary-mandibular fracture component to the skull.

produce the latter slight pressure on the parotid gland may be necessary. The appropriate antibiotics should be administered. If incision and drainage are necessary, a vertical skin incision should be made along the anterior border of the external ear. The anterior border of the wound is retracted and by blunt dissection in a horizontal plane, in order to avoid the facial nerve. entrance is gained into the gland through the capsule. Drains are inserted. the wound closed in part and a pressure dressing applied.

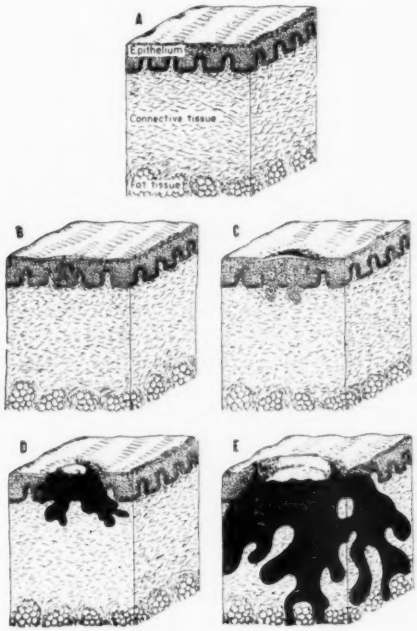

Fig. 4—Diagram of histogenesis of a carcinoma correlated with gross clinical findings. A, normal. B, subclinical stage (incipiency—carcinoma *in situ*). C, early clinical stage (nodule). D, advanced clinical stage (ulcer). E, far advanced clinical stage (Metastasis). [From Sarnat, Bernard G. and Schour, Isaac: Oral and Facial Cancer. The Year Book Publishers, Inc., Chicago, Ill. (1953)].

Chronic suppuration is found most frequently in the submaxillary salivary gland. This is usually found associated with calculi or mucus plugs within the gland, duct or both. Depending upon the size, location and number of calculi, partial or complete obstruction of salivary outflow may occur. Swelling and pain in the gland and surrounding area occur at mealtimes because of the accumulation of the increased amount of saliva produced. Where possible stones in the duct should be removed intraorally. Sometimes with smaller stones, dilatation of the duct may aid their being expelled. With removal of

the obstruction to salivary flow, the infection will usually subside. When the calculi are within the gland, it may have to be extirpated by the extraoral submaxillary route.

Traumatic lesions are divided into acute and chronic. Acute include:—Facial Fractures:—Acute or chronic trauma may produce lesions of the soft tissues and/or jaws. Injuries of this region are of more than ordinary significance since, if they are not properly treated at the time of infliction, they are apt to leave deforming scars and serious functional impairment. Subsequent treatment may require multiple plastic surgical procedures, after which the final result may still leave much to be desired.

Sudden external forces to the face as a result of a vehicular accident, fist blow, missile, or fall may cause fractures involving the mandible, maxilla, zygoma, nasal or other facial bones. Diagnosis and treatment of a facial bone fracture is as much of an emergency as a fracture of a long bone. When a jaw fracture is sustained, the teeth and supporting structures are also frequently involved and the organisms in the oral cavity gain access through the torn mucous membrane to the site of fracture. Consequently, jaw fractures involving the teeth are compound fractures. The most common cause of mandibular fracture is probably fist blows. Children who fall from a bicycle or porch may sustain a broken jaw. Occasionally, during extraction of a lower third molar, the mandible is fractured. Fractures also occur where pathologic processes are present in bone. Thus, the etiologic agent may be in local conditions a cyst, neoplasm or osteomyelitis or in a systemic condition, hyperparathyroidism.

The signs and symptoms of a fracture are: deformity, malocclusion, pain, anesthesia, paresthesia, hemorrhage, abnormal mobility, trismus and swelling. Roentgenographs of the entire mandible, maxilla and other facial bones should be taken, lest an unsuspected fracture be missed. The x-ray picture is invaluable as relates to the site, direction, comminution, and number of fractures. It is, however, of little value as pertains to the stage or degree of healing.

Before treating a patient with a facial injury it is important to remember that he must be in satisfactory general condition and able to withstand the surgical procedure. One must determine immediately whether anything is obstructing the trachea, whether there is active hemorrhage and whether the patient might be in shock. Injuries to the skull, cervical spine, chest, or viscera must also be considered.

Specifically, however, treatment of the fracture resolves itself into bringing the fragments back into normal position as soon as possible. Dental occlusion and lack of deformity are our guide. Most of these fractures can be treated by closed manual reduction. Sometimes, in order to get satisfactory reduction of the fragments, it is necessary to expose the fracture site. In jaw fractures the fragments are maintained in position by dental fixation and wiring of the jaws

or by skeletal fixation wherein the bone itself is utilized. Sometimes a combination of both dental and skeletal fixation is used (Fig. 3).

In maxillary fractures the jaws are wired together, in occlusion, and fixed by means of subcutaneous wires to the skull (infraorbital plate of bone, zygomatic arch, etc.) (Fig. 3). Zygomatic fractures may be reduced and fixed by the intra- or extraoral route. Fractures of the nasal bones are usually reduced through the endonasal route. Intra- and extranasal pressure dressings are then applied.

Postoperative care is concerned with diet, oral hygiene, care of the appliance and control of infection. When the jaws are wired together, it is important to see that the patient obtains an adequate diet in terms of consistency, calories and essential foodstuffs. Addition of calcium and Vitamin D to an adequate diet will not cause the fracture to heal any more rapidly. Intermaxillary fixation should be removed if the patient is going to vomit.

Soft tissue injuries:—The same force which produces a facial fracture may also cause widespread injury to the oral and facial soft tissues in the form of contusion, laceration, avulsion, and introduction of foreign material. Because the lips and cheeks are sometimes severely impressed against the teeth, deep irregular lacerations in these areas may also be sustained. Bleeding should be controlled. Early primary repair, where possible, is essential. The wound should be cleansed by gentle irrigation with a warm normal saline solution. All accessible debris, including broken teeth, glass and dirt, should be removed to decrease the possibility of infection and unsightly tattoo. Every effort should be made to preserve as much of the damaged but viable tissue. Irregular margins may be trimmed minimally. The wounds are closed in layers. Drainage is seldom necessary if good hemostasis has been obtained. A properly applied pressure dressing will facilitate healing. Antibiotics and tetanus antitoxin or a booster should be administered.

Chronic lesions:—The chronic irritation of the gingivae of the alveolar ridge or buccal sulcus by a poorly fitting artificial denture provokes a hyperplasia of the tissue. This same response occurs when there is a lack of adaptation of the upper artificial denture to the palate. Removal of the prosthesis for several weeks will permit the hyperplastic tissue (*granuloma fissuratum*) to shrink either considerably or completely. Excision of the remaining excessive tissue and accurate approximation with sutures is then less of a problem. It is important when excising the many folds of hyperplastic tissue to preserve the buccal or labial sulcus, so that a well adapted artificial denture can be constructed.

For example, a satisfactory artificial lower denture cannot be made for a patient because of a deficient gingival labiobuccal sulcus, as a result of resorption of alveolar bone, trauma, necrosis, or burns. One method whereby the

sulcus can be deepened is by incising the desired amount and covering the raw surfaces with a skin graft to prevent them from healing together.

Tumor and tumor-like lesions:—Since cancer is the most important diagnosis to rule out, any lesion should be considered to be such until proven otherwise. On this basis all of the lesions found within the oral cavity and on the face or associated with these areas, which must be considered in the differential diagnosis, can be classified into the following three groups: 1. noncancerous, 2. precancerous and 3. cancerous lesions.

In addition to the tumors found elsewhere, the oral cavity also gives rise to specific tumors arising from the tooth-forming organs. Thus, two types are found: 1. those which are dental in origin and 2. those which are nondental in origin. It is of interest to note that tumors which are dental in origin are rarely malignant.

Noncancerous lesions:—Benign neoplasms and tumor-like lesions of the oral cavity can be conveniently grouped into: 1. those related to soft tissue and 2. those related to bone (Table I).

Among those related to soft tissue are:—Cystic:—The benign soft tissue lesions are principally solid (epithelial and connective tissue), except for those cysts which arise from mucous glands, particularly from the mucous membrane of the floor of the mouth, cheek and lip. After reaching a certain size these cysts will rupture spontaneously and tend to disappear temporarily, only to return after the opening has closed.

Solid:—The papilloma, an epithelial neoplasm, occurs on either the tongue or mucosal surface of the mouth. When subjected to trauma during mastication and speech and while still benign, it is a relatively simple surgical procedure to remove the papilloma. Such early treatment is recommended. The adenomas are not common. The mixed tumor or pleomorphic adenoma may occur in the parotid salivary gland, the submaxillary salivary gland, the palate, lip, cheek, or tongue.

The benign connective tissue tumors may occur wherever the particular tissue of origin is present. Treatment of these lesions is similar to those found elsewhere in the body.

Noncancerous lesions of the bone include those nondental in origin:—The solid central benign lesions of the jaws are similar to those found in bone elsewhere in the body[3]. The nondental bone cysts are found most frequently in the maxilla and are located in regions of fusion of the palatal processes (Table I). The traumatic cyst, a result of trauma, is found in the mandible. It has no epithelial lining and the cavity may be empty or filled with the degradation products of blood. The diagnosis is usually made at the time of operation.

Dental in origin:—In addition, a group of tumor and tumor-like lesions which are dental in origin are also found within the jaws. They may be grouped into the solid type (ameloblastoma, odontoma and cementoma) and the cystic type (follicular, dentigerous, radicular cysts, and the cystic ameloblastoma). None of these ever becomes malignant with the possible but rare exception of the ameloblastoma.

Solid lesions include:—Odontoma:—The odontoma may contain from one to many irregular calcified bodies, which are composed of enamel, dentin and cementum arranged in bizarre patterns. This tumor, which is actually a secretory product, develops when the tooth-forming organs are active and its growth stops with the cessation of activity of the formative cells. Clinically, many of these growths are first found during routine roentgenographic examinations.

Ameloblastoma:—The ameloblastoma is derived from the cells of the odontogenic epithelium (dental lamina, enamel organ)[4]. It is found most frequently in the mandible and much less in the maxilla. The ameloblastoma is a benign neoplasm which seldom becomes truly malignant and metastasizes. A better known characteristic of this tumor is its persistence and tendency to "recur" after operative intervention, probably because of the small peripheral buds which are missed in the bone marrow spaces. The ameloblastoma, which is most frequently seen in young adults, is characterized by a slow progressive swelling, usually near the angle of the mandible. There is frequently a history of removal of one or more teeth from the area and of repeated surgical attempts to remove the tumor. Secondary infection of the tumor and fistulous tracts leading to the oral cavity or skin are not uncommon complications. The roentgenogram serves as a valuable adjunct in the diagnosis of radiolucent lesions of the jaw. The final diagnosis, however, depends on the gross and, particularly, the microscopic examinations.

Cystic lesions include:—Follicular and dentigerous cysts:—The follicular cyst is a result of the cystic degeneration of the tooth germ. When the crown of a tooth is included within the cyst, it is known as a dentigerous cyst. These are usually discovered first on routine roentgenographic examination.

Radicular cyst:—The radicular cyst is environmental rather than developmental in origin and occurs at the root end of the adult tooth. The pathologic process is that of caries of the enamel and dentin, with subsequent exposure and death of the dental pulp. This infection spreads to the root end of the tooth and, eventually, causes the formation of a granuloma. Sometimes the granuloma undergoes cystic change to form a root end cyst, which may become secondarily infected and, eventually, drain. On the roentgenogram both the periapical granuloma and root end (radicular) cyst appear radiolucent, and one is not always able to distinguish between them.

"Precancerous" lesions:—The term "precancerous" must be used with certain qualifications. It is well known that cancer of the mouth is sometimes found

associated with leukoplakia, papillomas, chronic ulcers and fissures. The atrophic mucosa of the oral cavity and pharynx associated with Plummer-Vinson syndrome and Vitamin B deficiency is also predisposed to cancer. In the cancer-susceptible patient these lesions, after adequate irritation, may undergo malignant change. Not all, however, will become cancer, so that to use the term "precancerous" may be condemning a benign lesion. It is impossible to determine which of the precancerous lesions will remain benign and which will become malignant. Therefore, it is good practice to remove at once for microscopic examination those apparently benign lesions which are subjected to chronic irritation or which show signs of change.

Leukoplakia, a chronic whitish lesion, is found on the buccal mucosa, palate and tongue. It has also been found on the vermilion zone of the lips and elsewhere on the mucous membrane of the mouth, pharynx and esophagus. Not all white lesions, however, are leukoplakia. Hyperkeratosis, lichen planus, moniliasis, and mucus patch and areas exposed to chemical and physical agents may also have the appearance of white patches.

Leukoplakia may occur either as a single small spot or cover large areas such as the entire dorsal surface of the tongue. Its borders are usually irregular. The consistency and color of the surface may vary from one which is quite thin, smooth and barely palpable and bluish-white (Grade I) to one which is quite thick, leathery, ridged, warty, and yellow-white (Grade IV). In this latter type, chronic fissures or ulcers are sometimes seen. If the lesion is small enough it can be completely excised and examined microscopically for possible malignant change. Larger suspected lesions can be biopsied before treatment is instituted. Excision with direct closure or application of a skin graft or electrocautery destruction are accepted methods of treatment.

The majority of cases of leukoplakia probably do not develop into cancer. Epidermoid carcinoma, however, is sometimes found in its vicinity. Patients with leukoplakia should be warned of the possible danger. Any patients with leukoplakia should be checked for the four "S's": 1. smoke, 2. spirits, 3. spices 4. syphilis. They should discontinue the use of all oral irritants such as tobacco alcoholic beverages, highly seasoned and hot foods, and should report for periodic check-ups. The diet should be supplemented with vitamins, if necessary, particularly Vitamin B-complex and, possibly, Vitamin A. If the patient is found to have syphilis, specific treatment should be instituted, especially since luetic glossitis, leukoplakia and carcinoma of the tongue are frequently found associated with each other.

Cancerous lesions:—Although oral malignancies have been reported at birth, they are seldom found before the fourth decade, the majority occurring in the fifth to seventh decades. Epidermoid carcinoma is the most common lesion and it occurs predominantly in the male. The etiology of oral cancer must be considered on the same basis as that in the rest of the body. The occur-

rence of carcinoma of the mouth in association with leukoplakia, avitaminosis B, Plummer-Vinson syndrome, and syphilis is known. Chronic irritation, as a result of smoking, rough teeth or dental restorations or biting may sometimes be an initiating factor. Surely, wherever possible, these conditions should be corrected, even if only to improve oral hygiene.

Carcinoma:—These malignant epithelial neoplasms arise locally either from the stratified squamous epithelium of the oral mucous membrane or from the glandular elements. The adenocarcinoma is found most often in the parotid and the palatal glands. The most malignant of all tumors is the melanoma, which grows rapidly and metastasizes early. It is coal black in appearance. It may be seen on the gingiva or the buccal mucosa.

Some secondary oral carcinomas have metastasized from a primary lesion in a distant organ. Thus, carcinoma of the prostate, thyroid, kidney, breast, rectum, and lung have a tendency to metastasize to bones and may, therefore, metastasize also to the jaws. The histologic picture of the primary growth is often duplicated in the metastatic lesions. These secondary tumors, because they are metastatic, are usually located within the center of the jaw. Diagnosis of the primary tumor is sometimes made only after histologic examination of the metastatic lesion.

Sarcoma:—These malignant nonepithelial neoplasms arise from the more deeply situated tissues of the oral cavity and adjacent structures. Most sarcomas arise from the tissues of the bones. Consequently, the tumors are frequently centrally located within a bone and lead to its enlargement. This enlargement results from destruction of the bone from within and apposition of new bone on the outer surface and leads to asymmetry of the part. Because of pressure on nearby nerves, pain may be one of the earlier complaints. Sarcomas usually occur in the younger age groups (first to fourth decade). They grow rapidly and, as a rule, the prognosis is not good. Occasionally, a sarcoma in some remote part of the body, such as the femur, may metastasize to the jaws. Consequently, one must be on guard not to miss this possibility. In leukemia the gingiva may be enlarged and show characteristic changes which, at times, constitute one of the earliest diagnostic signs.

General principles of surgical treatment:—The method by which surgery accomplishes its purpose is obvious. It requires either the complete removal or destruction of all the cancer cells. Treatment can be accomplished both more readily and more satisfactorily when the growth is small and localized (Fig. 4). When the growth is large and has spread, either locally or to a distant source, complete removal is more difficult and less successful.

Surgical treatment is required not only of the primary oral lesion but also of the cancer which has spread beyond the oral cavity. Because carcinoma travels through the lymphatics, surgical procedures have been devised to remove

these tissues. Consequently, a neck dissection, a procedure whereby all cancer-bearing tissue originating from either the mouth or face is removed, may sometimes be a more formidable procedure than the local removal of the primary lesion.

Cancer of the lip and skin of the face spreads to the neck late and infrequently. Because the metastases from the lip are usually limited to the upper neck, sometimes in both submental and submaxillary areas, a bilateral suprahyoid neck dissection may be performed. Because cancer of the floor of the mouth, tongue and tonsil tend to spread to the neck earlier, more frequently and more extensively than cancer of the lip, more neck dissections are necessary with such lesions. The complete unilateral and, occasionally, a complete bilateral neck dissection will be required. There is no unanimity of opinion concerning the time of, and the indications for, neck dissection.

Summary

The systematic examination of the oral cavity has been a neglected phase in medical practice. No part of the digestive system is more accessible to complete examination than the oral cavity. Visual, digital and roentgenographic examination as well as biopsies are readily performed and often yield significant information in regard to not only local but also systemic disease.

The diagnosis and surgical treatment of the lesions of the oral cavity and related structures are, essentially, the same as that of the rest of the body. The same general surgical principles, with certain variations, must be observed in regard to preoperative, operative and postoperative care. The ultimate goal is to obtain as near normal function and appearance. Frequently, to attain this goal, various plastic surgical procedures are essential either at the time of the initial, or at subsequent, operations.

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Discussion

Dr. I. Snapper (Brooklyn, N. Y.):—In connection with the excellent presentation by Dr. Sarnat it seems appropriate to state that the x-ray diagnosis of osteolytic lesions in the mandible is well nigh impossible. Since even in the adult red bone marrow is found in the mandible, the jaw is liable to be involved in many different proliferating processes, especially lymphomas, myeloma, malignancies, etc. In all these cases the x-rays only show an osteolytic lesion and the differential diagnosis completely depends upon the results of the biopsy. Even the examination of the biopsy alone may not be sufficient for the diagnosis. Any giant cell tumor in the skull, but especially in the jaw, often indicates the presence of a generalized disease, that is hyperparathyroidism. Whereas a giant cell tumor in an extremity may or may not be a sign of hyperparathyroidism, a giant cell tumor in the skull or in the jaw is nearly always a sign of hyperfunction of the parathyroids and requires a very careful examination of calcium and phosphate metabolism.

It is very interesting to learn about the excellent results of the plastic operations of deformities of the face. Such patients often consult the gastroenterologist for a specific complaint, that is for anorexia. In such cases complete and careful examination of the gastrointestinal tract hardly ever reveals an anomaly which could explain the poor appetite. Operations as reported by Dr. Sarnat, however, immediately solve this problem because after operation the appetite returns. In other words the operation solves the psychological problem of these patients. They are restored to normal life and their appetite returns.

One lesion in the mouth which is of special importance to gastroenterologists should be mentioned. Sometimes the source of intestinal hemorrhages of unknown origin can be solved by careful examination of the oral cavities or by biopsy of the gingiva. In this connection telangiectasia must of course be mentioned. One of the other causes of intestinal hemorrhage is primary amyloid. In this condition amyloid is deposited in the musculature all through the body as in the tongue, heart, pharynx, intestine. It is also present in the subcutis and the skin, and as a matter of fact it may involve any other organ because widespread amyloid degeneration of the musculature of the small arteries is a common sign of this disease. This primary amyloid nearly always occurs as a complication of multiple myeloma but is occasionally found in patients who do not suffer from myelomatosis. Primary amyloid should be distinguished from the amyloid which develops after chronic ulceration and suppuration because the latter is mainly localized in the spleen, liver, kidneys and adrenals. Intestinal hemorrhage by amyloid is only present in primary amyloid. In this ailment chronic swelling of the tongue, so-called macroglossia, is often the first sign. Frequently small reddish tumors consisting of amyloid can be seen in the mucous membranes of the mouth. Even in the absence of macroglossia or

visible tumors, however, biopsy of the gum may prove the presence of primary amyloid localized either in the submucous area or around the blood vessels.

It follows that the gastroenterologists must stay in close contact with the dental and oral surgeons whose primary interests are localized in the oral cavity.

Question:—I would like to ask the speaker one question about epulis. How often does epulis become malignant and metastasize to the scalp?

Dr. Sarnat:—The use of the term "epulis" should be more specific. "Epulis" means, essentially, just a growth on the gum. Consequently, there are a number of types of epulis (hemangioma, fibroma, giant-cell type, etc.).

In answer to your question, how often does epulis become malignant, only as often as it is a malignancy. By and large, again using the term generally, I would say that very few of the conditions we term epulis are malignant, but there are a certain number of malignancies that look like an epulis.

Does that answer your question?

Questioner:—No.

Dr. Sarnat:—Do you want to be a little more specific?

Questioner:—This case was pathologically a case of common epulis. Then the recurrence occurred in the mouth and it occurred in the sinus and finally went behind the eye and pushed the eye forward, with metastasis to the top of the skull. Then the diagnosis was changed from the ordinary, plain epulis to giant-cell sarcoma by five pathologists.

Dr. Sarnat:—I am not a pathologist, but I would say that a histopathologic diagnosis of "epulis" should not be made. A specific microscopic diagnosis should be given as to whatever that particular tumor is. In this instance they eventually said it was a type of giant-cell tumor.

How often does epulis become malignant? Only as often as there is malignancy. It is a nonspecific term, as far as I am concerned. Epulis should be dropped and not used. They should diagnose it specifically for whatever that growth happens to be.

THE SPECIFICITY OF THE PROTECTIVE ROLE OF THE PYLORIC ANTRUM IN EXPERIMENTALLY INDUCED PEPTIC ULCERATION*†

ROBERT S. KAPLAN, M.D.‡

and

DAVID STATE, M.D.

Los Angeles, Calif.

Dr. Wangensteen has reported that when a segmental resection of 75 to 85 per cent of the acid secreting gastric mucosa is done with anastomosis of the remaining gastric pouch to the pyloric antrum *in continuity*, there have been no recurrent ulcers in his patients[1]. The work of Dragstedt and coworkers has shown that a hypersecretion of acid results when the antrum is removed from

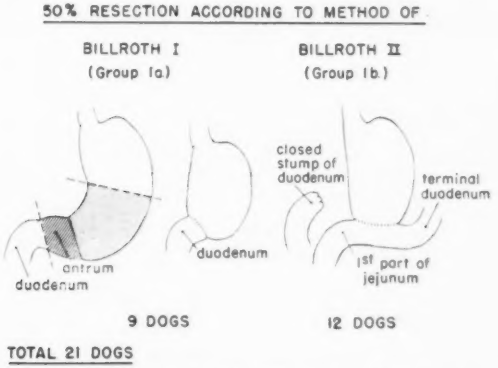

Fig. 1—Group I, 50 per cent resection with Billroth I and II anastomosis—control series—ulcer incidence 71.4 per cent.

its normal continuity in the gastrointestinal tract and anastomosed to the colon[2]. It is felt by them that the resulting hypersecretion of gastric juice is due to overstimulation of the so-called "antral phase" of gastric secretions. We feel that in view of certain known physiological qualities of the pyloric antrum and our own studies, that the pyloric antrum not only is of great importance in the production of gastric acid, but is also of importance in the inhibition of excessive

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‡National Cancer Institute Trainee.

From the Department of Surgery, Cedars of Lebanon Hospital, and the University of Southern California, Medical School.

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acid secretion, if left in normal continuity. The antral exclusion operation, where the antrum is left in, but excluded from normal continuity with the gastrointestinal tract, fell into disrepute following the sad experiences of Finsterer, von Eiselberg and others, for the recurrence of ulcers were rapid. We feel this occurred because the antrum was not allowed to function in its normal physiologic manner, i.e., acid secreted by the stomach was unable to contact antral mucosa and prevent the further release of gastric acid. The present studies are related to the specificity of the apparent protective action of the pyloric antrum.

Method

Six groups of healthy mongrel dogs were operated upon. Those that were to have intestinal transplants, received intestinal antibiotics for several days prior to operation. The animals were anesthetized with intravenous sodium

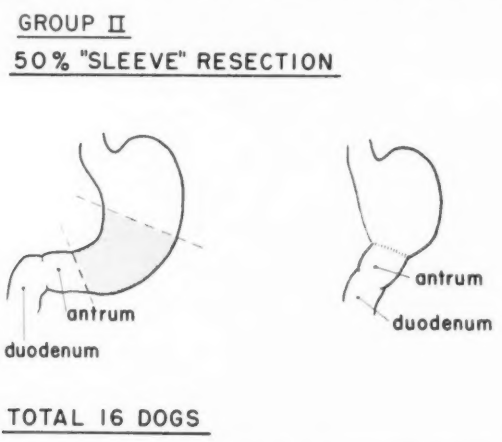

Fig. 2—Group II, 50 per cent "sleeve" resection of acid secreting mucosa followed by gastroantrostomy—ulcer incidence 12.5 per cent.

nembutal (15 mg. per lb. of body weight). Sterile operative technic was used. Postoperatively, the animals received intravenous fluids and antibiotics as long as was thought necessary.

Group I (Fig. 1) consisted of 21 dogs in whom a 50 per cent resection of the acid secreting gastric mucosa plus the antrum was done, according to either the Billroth I or II method. These were used as controls.

Group II (Fig. 2) consisted of 16 dogs in whom a "sleeve" (segmental) resection was done of 50 per cent of the acid secreting stomach. The residual gastric pouch was anastomosed to the antrum *in continuity*. No pylorplasty was done.

Group III (Fig. 3) consisted of 15 dogs in whom a 50 per cent "wedge" (pie) resection of the acid secreting mucosa was done. The lesser curvature was left intact. The cut edges of the greater curvature were re-approximated. The vagus nerve fibers along the lesser curvature were not disturbed.

Group IV (Fig. 4) consisted of 4 dogs from Group II and 5 dogs from Group III, who failed to develop ulcers while on daily histamine in beeswax injections over a period of 30 consecutive days. These dogs were re-operated upon and the antrum removed. Gastrointestinal continuity was restored by Billroth I or II technic.

Group V (Fig. 5) consisted of 7 dogs who underwent resection of the antrum, plus 50 per cent of the acid secreting mucosa. The antrum was replaced

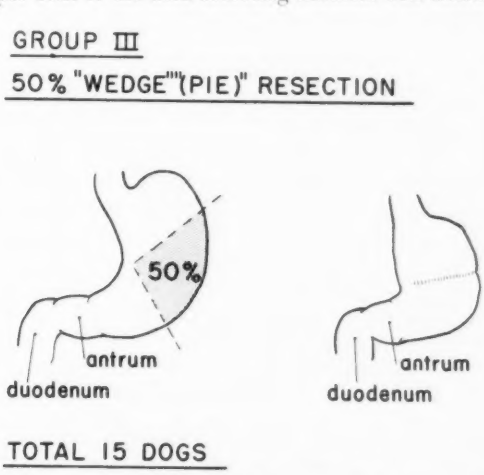

Fig. 3–Group III, 50 per cent "wedge" or "pie" resection of acid secreting mucosa followed by transverse closure of remaining stomach–ulcer incidence 6.6 per cent.

by a segment of jejunum taken from just beyond the duodenojejunal angle, and was of the same length as the antrum.

Group VI (Fig. 6) consisted of 12 dogs who had substitution of a segment of transverse colon for the antrum, following resection of 50 per cent of the acid secreting gastric mucosa plus the antrum.

One additional dog who had not had any surgical procedure was placed on daily injections of histamine in beeswax (30 mg. per day), according to the method of Code and Varco[3] merely to check the potency of our preparation. This dog died of a perforated duodenal ulcer on the 23rd day of injections.

In the operated animals, the amount of stomach resected was checked by weight at initial operation and at autopsy or sacrifice. These estimates showed good correlation indicating that a 50 per cent resection had been performed.

After a period of postoperative recovery of about 30 days, each of the dogs in Groups I, II, III, V and VI received 30 mg. of histamine base in beeswax by injection for 30 days or as long as they survived up to 30 days. At the end of the injection series, they were either autopsied or a laparotomy was done on them. Nine dogs from Groups II and III who showed no evidence of ulcer had the antrum resected secondarily with restoration of gastrointestinal continuity by the Billroth I or II method. These 9 dogs comprised Group IV who after a second postoperative recovery period of 30 days, were again subjected to the regimen of 30 days of histamine in beeswax.

Results

Our findings are summarized in Table I.

TABLE I

Group I	Controls (Billroth I & II)	21 dogs	15 ulcers	71.4%
Group II	"Sleeve" resections	16 dogs	2 ulcers	12.5%
Group III	"Wedge" resections	15 dogs	1 ulcer	6.6%
		31 dogs	3 ulcers	9.6%
Group IV	Re-resections	9 dogs	8 ulcers	89%
Group V	Jejunal Transplants	7 dogs	7 ulcers	100%
Group VI	Transverse colon transplants	12 dogs	8 ulcers	66%

Comment

In 1906 Edkins[4] found that an extract of antral mucosa, if injected intravenously, would cause the secretion of acid by the parietal cells. Later in 1909[5] he reported that the introduction of certain substances into an antral pouch that was closed off from the fundus resulted in the secretion of acid from the fundus. Edkins concluded that substances in ingested food acted upon antral mucosa causing the release of a histamine-like substance, which he called "gastrin". Edkins believed that the "gastrin" was absorbed into the bloodstream and acted upon the fundic cells causing secretion of acid.

From Dragstedt's laboratories[6] has come experimental evidence which lends much weight to Edkin's original theory. They have found that the mucosa of the antrum under proper stimulation releases into the blood stream chemical substances which cause hypersecretion of gastric juice. Under other conditions, this same antral mucosa when properly stimulated has been found to inhibit the secretion of acid. Acid substances were found to inhibit gastric secretion when placed in excluded antral pouches. They further reported that in dogs with vagus denervated gastric pouches, the secretion of acid was greatly reduced when the antrum was excised.

As mentioned previously, von Eisenberg, Finsterer and Devine have shown that the "antral exclusion" operation was a poor one for peptic ulcer, for it was followed by almost 100 per cent stomal ulceration. We feel that this resulted from the fact that acid secretions were unable to contact the excluded antrum and thus mediate inhibition on further acid secretions. The same reason probably accounted for the resultant hypersecretion in Dragstedt's series, wherein the antrum was removed from its normal *continuity* in the gastrointestinal tract and anastomosed as a diverticulum to the colon. Here not only was acid unable to come in contact with the antral mucosa, but the antrum was possibly being continuously stimulated by alkaline substances and pressure.

Harvey and Bensley in 1912 and later Ivy and Oyawa[7] showed that the secretions of the antrum do not contain any acid. Sokolow[8] showed that the

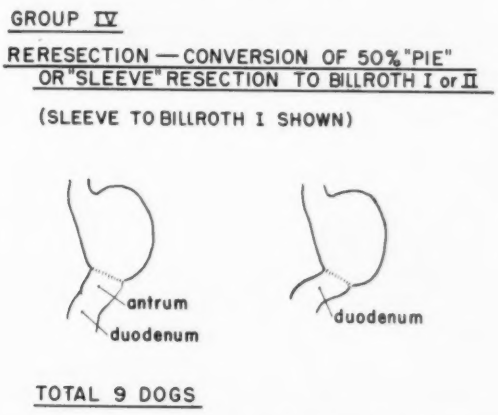

Fig. 4–Group IV, re-resections of 50 per cent "pie" or "sleeve" resections with Billroth I and II anastomosis–ulcer incidence 89 per cent.

introduction of 0.5 per cent hydrochloric acid into the stomach markedly reduced the secretion of acid from a Pavlov pouch. We feel that this inhibitory action of the contact of acid on antral mucosa is the manner in which the pyloric antrum protects our animals from developing ulcers. In our experiments, dogs in Groups I, II, III and IV would seem to indicate that leaving the antrum *in continuity* protects dogs from histamine-induced ulceration.

There are a number of ways in which this protective action may be brought about. It may be specific or nonspecific. By specific, we mean that the inhibition of gastric secretion by the antrum may be due to a decreased liberation of gastrin, or possibly, due to a specific inhibiting hormone, which is liberated when gastric acid contacts antral mucosa. These possibilities are being investigated at the present time.

The nonspecific protection of the antrum may be due to 1. its alkaline secretion or 2. to its spatial relationship between the acid secreting mucosa and the duodenum. By substituting a segment of transverse colon for the antrum, the spatial factor was replaced. By substituting a length of jejunum for the antrum, both the spatial factor and the alkaline juice secreted by the antrum have been replaced for the upper jejunum secretes an alkaline juice similar to the antral secretions. The fact that 66 per cent of the transverse colon transplants and 100 per cent of the jejunal transplants developed ulcers, while less than 10 per cent of the animals developed ulcers when the antrum was left *in continuity*, is strong presumptive evidence that the protective action of the antrum is a specific function of the antrum.

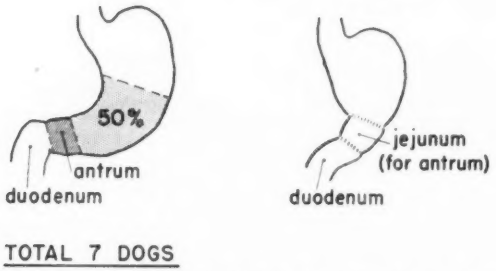

Fig. 5—Group V, 50 per cent "sleeve" resections of acid secreting mucosa with substitution of antrum by jejunum—ulcer incidence 100 per cent.

The incidence of almost 10 per cent ulcer formation in our dogs that had only 50 per cent resection of the fundus, would seem to contraindicate this procedure in man as a definitive surgical procedure. Kelly[9], however, has reported that "sleeve" and "wedge" resections of 75 per cent of the acid secreting mucosa completely protect dogs from histamine-induced ulceration.

Wangensteen[1] has reported on 90 patients that have had 85 per cent resection of the acid secreting mucosa by "sleeve" or "wedge" resection without development of a recurrent ulcer. We have operated upon 38 patients utilizing similar technics removing 75 per cent of the acid-secreting mucosa. We have had no fatalities and there has been no evidence of recurrence. Our longest follow-up is only 3 years, but the initial response is pleasing. The usual complications of conventional gastric resections appear definitely lessened. Of the 38 patients operated, only one instance of dumping syndrome was noted, and

that improved with time. Weight gain is almost the rule, and the return to work is rapid.

In 1929, Connell[10-14] first recommended a procedure which he called a "partial fundusectomy". He suggested that this allowed for the "direct minimization of acid secreting fundus but with retention of the distal stomach and its favorable secretions and motor functions". He further stated that "such a procedure becomes logical and practical when it is realized that the stomach is, from physiologic, anatomic, embryologic and evolutionary points of view, a double organ". He indicated that removal of part of the fundus and allowing the antrum and pylorus to remain with normal secretory and motor functions seemed a desirable improvement over procedures which removed or excluded the antrum. (If one can use his illustrating diagrams as a guide to the amount

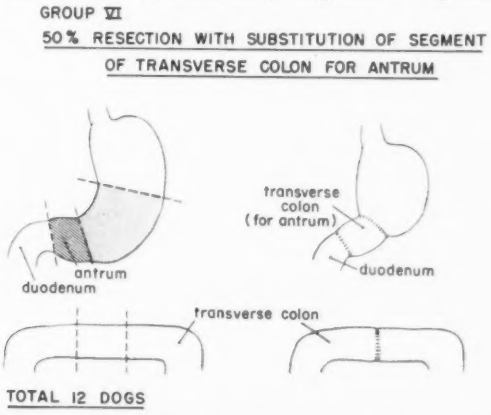

Fig. 6–Group VI, 50 per cent "sleeve" resections of antral mucosa with substitution of antrum by transverse colon–ulcer incidence 66 per cent.

of acid secreting mucosa that he resected, then his operation appears similar to our 50 per cent "wedge" resection.) In Wangensteen's reported cases, and in our own cases done on humans, we have resected at least an additional 25 per cent of the acid secreting gastric mucosa. Connell has reported his results on 25 patients, 19 of these had "satisfactory" results. Six were reported as having unsatisfactory results. It is to be noted that of these 6, 1 died on the 14th postoperative day of uremia and another died on the 5th postoperative day of intestinal obstruction at the site of a prior appendectomy. Of the other 4 unsatisfactory results, one had a second operation where additional acid secreting stomach was removed, and a 4-year follow-up showed he was doing satisfactorily. Connell suggests that his unsatisfactory results were due to inadequate removal of acid secreting fundus.

Berne[15] reported in 1954 that he had carried out a procedure of removal of a large wedge of the body of the stomach. He combines this with vagotomy

and pyloroplasty and apparently has achieved satisfactory results. He further stated that the ultilization of his procedure "involves the assumption of a basic concept that less drastic antiulcerogenic effects are necessary to cure duodenal ulcer, than to prevent jejunal ulcer". We feel that the "wedge" or "sleeve" resection is not only achieving good results, but that the operative technic is less difficult than the Billroth I or II type of resection. No problem is encountered in closure of a difficult duodenal stump and no attempt is made to remove the ulcer. If some stenosis of the pylorus is present, a Heineke-Mickuliz pyloroplasty is performed. Otherwise, nothing is done except to remove a wedge or sleeve of 75 per cent of the acid-secreting mucosa. Because the antrum comprises about 20 per cent of the total stomach, this means that 40 per cent of the total stomach is left *in situ* after resection. This provides an adequate gastric reservoir, normal digestion, and normal emptying.

Summary and Conclusions

Six groups of dogs were operated upon comprising a total of 80 dogs. Other controls and other types of investigative procedures have been done, but are not ready for presentation at present. Our control group consisted of 21 dogs having either a Billroth I or II type of 50 per cent gastric resection. They showed a 71.4 per cent incidence of ulcers. Of 31 dogs having "wedge" or "sleeve" resections, ulcers occurred in only 9.6 per cent. Nine dogs had re-resections following a prior "wedge" or "sleeve" 50 per cent gastric resection. At the second operation, the antrum was resected and a Billroth I or II anastomosis performed. Following the second operation, an ulcer incidence of 89 per cent was found.

Seven dogs underwent 50 per cent gastric resection plus resection of the pyloric antrum with substitution of a loop of jejunum of the same length as the pyloric antrum. All of these animals developed ulcers. Twelve dogs had transverse colon substituted for antrum following resection, and 8 of these animals developed ulcers for an incidence of 66 per cent.

We have concluded that the pyloric antrum, when left *in continuity,* exerts a protective effect against experimentally induced peptic ulceration in dogs. Further, it would appear that this protective action of the antrum is specific, for when a length of transverse colon or a loop of jejunum is substituted for the antrum, it fails to protect against peptic ulceration in our experimental animals.

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Discussion

Dr. Owen H. Wangensteen (Minneapolis, Minn.):—It was a real pleasure for me to have the opportunity of learning this paper because these ideas, in many particulars, run quite parallel to my own.

In fact, at the AMA meeting in 1951 in Atlantic City, Dr. Ravdin, who was then Chairman of the Surgical Section, knowing of my interest in this problem, felt that I should present my experience with segmental resection before that Section. I demurred, but as many of you know, Dr. Ravdin is quite persuasive. In any case, I found myself listed presently for such a presentation. Such a meeting in my experience is not an acceptable springboard for the presentation of a controversial matter. And, as I had supposed, I got a good drubbing. In fact, failure of the procedure was predicted. My only defense was that I had far greater confidence in evidence than in testimony, and that I was willing to allow Time to be the final arbiter as to whether the procedure had merit.

Dr. Kaplan has come forward with additional evidence that segmental gastric resection is a good operation. Dr. Wirts suggested I say something on the historical aspects of the origin of this procedure. Mikulicz of Breslau first devised segmental resection. He coined the term "segmental resection", which I think is a preferable term to the designation "sleeve resection". Mikulicz devised and gave up the operation all in the year 1897. He concluded the operation had little merit. Then the operation was successively taken up by Bernard Riedel (1909) of Düsseldorf and by Erwin Payr of Leipzig (1910). At the German Surgical Congress in 1912 segmental resection was cordially endorsed by several surgeons. Marquardt at the same session expressed the desire to place at least one instance of failure of the procedure in the record.

The last kind words said for the procedure were spoken by Judd and Lyons at the 1922 meeting of the American Surgical Association (Ann. Surg. **76**:409, 1922). Most surgeons of my generation, however, had never seen the operation done, nor had I.

When I took up with the operation 50 years after its abandonment by Mikulicz, it was essentially for two reasons: 1. the great technical difficulty presented by large supraduodenal ulcer craters in the Billroth II operation.

2. because of the rather high incidence of the dumping syndrome following the Billroth II operation—circumstance to which Dr. Kaplan alluded. In a very difficult duodenal ulcer, one cannot do a Billroth I operation; and the Billroth II procedure in certain large ulcer craters is an unsafe operation, in that the duodenal closure can be extremely difficult to accomplish. When the ulcer perforates into the pancreas, it is a simple matter; the anterior wall of the duodenum can be buttressed against the pancreas. If, however, the ulcer crater extends out over the common bile duct, the technical problem of closing the duodenal wall securely can be a very difficult, if not an impossible technical problem.

My early experience with segmental resection was not too happy. My first patient did very well. The next three patients had gastric retention, and I found it necessary to do a subsequent complemental pylorotomy. It finally dawned on me that the reason earlier surgeons had bad luck with the operation was that transverse section of the stomach denervates the antrum. The inclusion of a Heineke-Mikulicz pylorotomy in the initial operation resolved the problem completely, and I have continued to add it routinely.

Approximately eight years have now gone by since I began wrestling with segmental resection. It is the only operation following which no recurrent ulcers have been seen in this clinic. That is a good deal to say for any operation for duodenal ulcer. Moreover, 90 such resections were done four years or more ago.

The Billroth operations are satisfactory operations for peptic ulcer, if done adequately. Such operations will protect against recurrent ulcer but the excision has to be in excess of the extent of the excision necessary in segmental resection.

The special point I tried to make in my presentation in 1951 (J.A.M.A. **149**:18, 1952) was that there is an important difference between *retaining* the antrum and *excluding* it as Eiselsberg first suggested in 1895. The great worth of Finsterer's papers in indicating the extent of the necessary excision in the Billroth II operation bespeaks the great importance of careful and painstaking observations. By 1934 Finsterer had come to the conclusion that it took a two-thirds excision in the Billroth II procedure to afford reasonable protection against recurrent ulcer.

In the segmental resection as I have done it, we denervated the antrum and found a complemental pylorotomy necessary to preclude the occurrence of gastric retention. One of my surgical associates, however, Dr. Donald Ferguson, Chief Surgeon at the Veterans Hospital, Minneapolis, has taken pains to avoid injuring the antral vagal twigs in dividing the antrum and thereby has found it possible to eliminate the Heineke-Mikulicz pylorotomy, save in the presence of duodenal stenosis. He has, however, already had one bona fide recurrence with segmental resection amongst 100 cases done within the past

three years. As I recounted earlier, no recurrence amongst 90 segmental resections done between four and eight years ago, has been seen in my clinic.

Because the dumping syndrome continued to be observed occasionally following the segmental resection, I began casting about for an additional surgical approach to the problem of duodenal ulcer. And before this group in 1952, I presented some preliminary observations upon tubular gastric resection, accompanied by transverse gastroplasty (Rev. Gastroenterol., **20**:611, 1953). This operation was essentially a variant of the linear type of subtotal excision of the acid secreting area of the stomach upon which I had published a note several years before (Surg., Gynec. & Obst. **70**:59, 1940). In turn, the operation can be described as an amplified Connell operation (Surg., Gynec. & Obst. **49**:696, 1929) or pie excision of the greater curvature as Dr. Kaplan alluded to it.

On many scores, tubular resection with transverse gastroplasty is a good operation. Already, however, we have observed two recurrences following performance of the procedure, and our experience in years is considerably less than with segmental resection. Our early experience with tubular resection seemed so promising that, we took up with it to the temporary exclusion of segmental resection. Because of these recurrences (2 in 200 tubular resections), however, we have abandoned it to return to segmental resection, which the experience of this clinic suggests is probably the best of available operations in the surgical management of duodenal ulcer.

About two years ago, we began to assess in the experimental laboratory upon dogs the response of isolated Heidenhain pouches to the ingestion of food following the various operations performed for peptic ulcer. Drs. Alan Thal and John Perry observed that the ingestion of 200 grams of cooked horsemeat following performance of segmental gastric resection elicited no response from the isolated Heidenhain gastric pouch of these dogs, if the antral vagal innervation was interrupted. When, however, pains were taken to preserve the antral vagal twigs, a definite, augmented response attended the ingestion of horsemeat. Moreover, following performance of tubular resection, in which the entire lesser curvature of the stomach is left intact, the ingestion of meat provoked regularly a keen response in the isolated Heidenhain pouch. This observation led us to believe that we would presently see clinical recurrence of ulcer following tubular resection in man for duodenal ulcer. It was not long before we had the opportunity to observe the validity of that prediction. Meanwhile, we have discontinued doing tubular resection in this clinic. We are trying to resolve the nature of the difference in response to these two procedures. It is quite clear, I believe, that division of the antral vagal twigs in segmental resection is desirable. Whether there are other factors still unknown in this observed difference in behavior remains to be elucidated. It should be remarked here, however, that division of the main vagal trunks following either segmental or tubular resection elicits a greatly augmented secretory response from the isolated Heidenhain pouch, even though the emptying of the vagotomized stomach seems not unlike

that of the dog's stomach prior to performance of the vagotomy. This obviously is an occurrence which needs further inquiry and study.

Experimental and clinical evidence are in complete harmony on the suggestion that segmental resection is an excellent operation for duodenal ulcer. In performing segmental resection currently, we leave only about a 15 per cent residual gastric fundic pouch; the antral remnant is about the same size. In other words, somewhere between a 65 and 70 per cent gastric resection is done.

More recent studies by Dr. Perry in the experimental laboratory in which he has been assessing the digestive power of the gastric juice from patients who have undergone various types of gastric resection for ulcer, suggest too that segmental resection affords maximal protection against recurrent ulcer. The cat's esophagus makes an ideal testing ground to observe the latent digestive power of gastric juice after operation because of the great susceptibility of the esophagus to injury by acid-peptic juice. This latter mode of inquiry would appear to provide an additional and useful safeguard in defining what the criteria of an acceptable operation for peptic ulcer in man are.

Chairman Wirts:—Thank you very much, Dr. Wangensteen. Before we take a break, I think Dr. Necheles has one brief announcement he would like to make.

Dr. H. Necheles (Chicago, Ill.):—I want to take this occasion, on behalf of the College and of the Research Committee, to thank the donors of these awards, The Ames Company, its president and its vice president, for the far-sighted help that they have given the College. I think this is a step in the right direction. Education in gastroenterology is terribly deficient all over the country. We have only a few places where it can be done. We have therefore inaugurated the program of giving awards and prizes and of having lectures of high standings.

We intend to extend our work and to bring fellowships and support to laboratories and clinical divisions, that will further the development and education in gastroenterology.

I want to take this occasion to congratulate Dr. Kaplan on his very fine paper. I want to remark how the pendulum of time swings in the physiology of the stomach. We learned first that the antrum must be removed because it produces gastrin. Now, within the last few years, we have learned that gastrin production can be inhibited, and that it is probably more important to leave the antrum in its physiological position rather than taking it out, or taking the mucosa out.

One thing which was not stressed, and I would like to mention, is the importance of the pyloric sphincter. I would hesitate, as a physiologist, to take out that sphincter, because it regulates the normal, successive, gradual, physiological emptying of the stomach, providing better digestion, better absorption, and less dumping.

RECENT EXPERIMENTAL AND CLINICAL EXPERIENCES WITH ANTACID THERAPY IN PEPTIC ULCER*†

LEONIDAS H. BERRY, M.D., F.A.C.P., F.A.C.G.

JONAS ADOMAVICIUS, M.D.

T. J. COLE, M.D.

ROBERT SCHOOP, M.D.

and

JUANITA PURNELL, R.N.

Chicago, Ill.

A survey made a few years ago indicates that physicians in the United States see more than 361,000 patients with peptic ulcer per month, and there are approximately four million ulcer patients at all times[1]. Although this disorder is not uncommon, the problems of its pathogenesis, treatment and prevention continue to baffle the most astute minds of the medical scientists and leave unanswered important questions of management for the clinician.

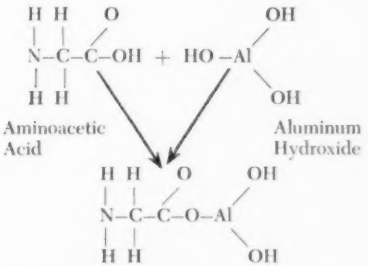

Fig. 1—Dihydroxy Aluminum Aminoacetate (Robalate—A. H. Robins Co.)

It is the purpose of this paper, therefore, to present recent controlled studies in peptic ulcer patients, using an aluminum salt, dihydroxy aluminum aminoacetate (DAA)‡, as an antacid.

A theoretically ideal antacid should be 1. nontoxic, 2. relatively insoluble or unabsorbable and therefore should not disturb the acid-base balance of the

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†From the Cook County and Provident Hospitals, Dept. of Medicine, University of Illinois College of Medicine, and the Cook County Graduate School of Medicine, Chicago, Ill.

‡Robalate® Tablets for this study furnished through the courtesy of William R. Bond, M.D., Director of Clinical Research, A. H. Robins Company, Inc., Richmond, Va.

These studies were supported by a grant from the A. H. Robins Company, Inc., Richmond, Va.

blood, 3. it should not cause "acid rebound" or secondary rise in gastric acidity, 4. it should exert a prolonged neutralizing effect in small doses, but should not suppress gastric acidity beyond a pH of about 3.5 to 5, 5. it should be palatable and relatively inexpensive, and 6. it should not have an excessively constipating or laxative effect. No antacid has as yet been devised which meets all of these criteria. Yet most of those named below have their good points. Many clinical investigators today agree that the aluminum products more nearly meet the criteria set forth for the ideal antacid.

A great mass of evidence accumulated over the years indicates rather convincingly that the suppression of gastric acidity with antacids is associated with relief of ulcer symptoms and the healing of the ulcer niche[2-5]. These effects may be dramatic and complete. These antacids (of which sodium bicarbonate

TABLE I

X-RAY STUDIES BEFORE AND AFTER DAA* TREATMENT
IN 99 ULCERATIVE LESIONS

X-ray Diagnoses Before Rx	
77 Duodenal Ulcers	(86 Examinations)
11 Gastric Ulcers	(15 ")
1 Gastrojejunal Ulcer	(1 ")
9 Hypertrophic Gastritis	(11 ")
1 Malignant Gastric Ulcer	(1 ")
X-ray Follow-up During and After Rx	
76 Duodenal Ulcers	(52 Examinations)
11 Gastric Ulcers	(8 ")
1 Gastrojejunal Ulcer	(3 ")
1 Malignant Gastric Ulcer	(2 ")
9 Hypertrophic Gastritis	(4 ")

*Dihydroxy Aluminum Aminoacetate

is the best example, however, may cause "rebound secretion" of acid gastric juice[6]. Other antacids, such as calcium carbonate and magnesium oxide, are relatively insoluble but the former is constipating and the latter may be quite laxative in neutralizing doses. Many other antacids, including the triple phosphates of calcium and magnesium, the exchange resins, protein hydrolysates and mucins, are in general use. A detailed discussion of the merits and demerits of all of these products will not be undertaken in this report.

METHOD OF STUDY

Clinical, x-ray and gastroscopic evidence of prompt and complete healing was evaluated. The incidence of recurrence in these groups of patients was observed over a period of 18 months. The importance of recognizing and separating the symptoms due directly to ulcer from those due to associated gastro-

intestinal disorders was emphasized. This is quite important and sometimes frequently overlooked.

Diagnostic:—The diagnostic criteria in this series were strict and consisted of laboratory and clinical evidence. It was not enough to merely have x-ray deformities. Each patient had an ulcer history indicative of activity. Many patients had repeated x-ray and gastroscopic examinations before treatment was started. Each patient kept a diary of symptoms during the work-up period in order to confirm or deny the original story. Occasionally, duodenal deformity

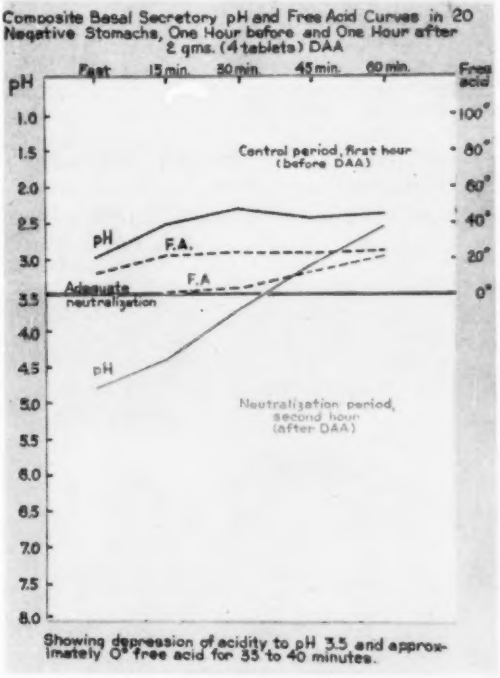

Fig. 2

was regarded as a healed scar or inactive ulcer because an ulcer syndrome was not present. The gastrointestinal symptoms in such cases were often indicative of functional bowel distress, associated cholecystitis or other gastrointestinal disorders.

Tables I and II show the number of x-ray and gastroscopic studies carried out in 99 ulcerative lesions consisting of 77 duodenal ulcers, 11 benign gastric ulcers, 1 gastrojejunal ulcer and 1 malignant gastric ulcer and 9 cases of hypertrophic gastritis.

TABLE II

GASTROSCOPIC STUDIES BEFORE AND AFTER DAA° TREATMENT IN 22 ULCERATIVE LESIONS

Gastroscopic Diagnoses Before Rx	
11 Benign Gastric Ulcers	(6 Examinations)
1 Malignant Gastric Ulcer	(1 ")
1 Gastrojejunal Ulcer	(2 ")
9 Hypertrophic Gastritis	(5 ")
Gastroscopic Follow-up During and After Rx	
11 Benign Gastric Ulcers	(7 Examinations)
1 Malignant Gastric Ulcer	(1 ")
1 Gastrojejunal Ulcer	(2 ")
9 Hypertrophic Gastritis	(4 ")

°Dihydroxy Aluminum Aminoacetate

The diagnosis and progress in healing were based upon multiple x-ray and gastroscopic examinations. In addition, fractional gastric analyses, blood, urine and stool examinations, as well as x-ray of gallbladder and colon, were done on all patients.

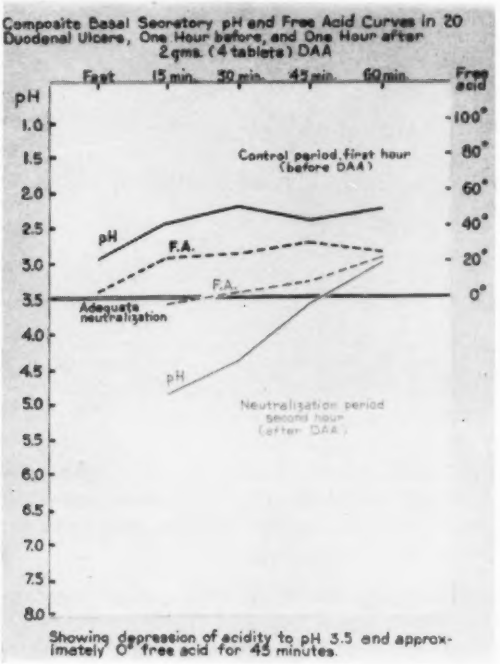

Fig. 3

Secretory:–In order to study the neutralizing effect of a selected antacid upon the gastric acidity of our cases of peptic ulcerative lesions, dihydroxy aluminum aminoacetate was chosen*. The principal group for our secretory studies consisted of 79 patients with peptic ulcerative lesions. Thirty patients with negative gastrointestinal tracts were used as controls. One hundred nine secretory experiments were run for two hours or more on 79 patients with peptic ulcerative lesions and 30 patients with negative gastrointestinal tracts. Aliquot portions of gastric secretion were removed periodically, measured and returned

TABLE III

GASTRIC SECRETORY STUDIES
WITH DIHYDROXY ALUMINUM AMINOACETATE†

Method:–Fractional Analysis–
1 hr. control period before DAA, 2 hrs. following.
Fractions returned to stomach during 2nd & 3rd hrs.

Determinations:–
pH (Beckman's Electric pH Meter)
Free Acidity (Beckman's Electric pH Meter)
Total Acidity (Beckman's Electric pH Meter)
Vol. in c.c.

No. Experiments with 2 gm. DAA–(86)–4 gm.–(23) Total	109
No. Fasting Basal Secretory Experiments	91
No. Fasting Histamine Secretory Experiments	18
Total	109

TYPES OF CASES

Duodenal Ulcers	67	
Gastric Ulcers	8	
Hypertrophic Gastritis	4	
Total		79
Negative Stomachs as Controls		30
Total Cases Used		109

†Robalate (A. H. Robins Co.)

to the stomach except for minimal quantities from which to determine electrometrically the pH, free and total acidities (Table III). Following a control period of 1 hour, 2 gm., and in a smaller group of cases, 4 gm. of dihydroxy aluminum aminoacetate were crushed in one-half ounce of water and washed through a Levin tube into the stomach with an additional half ounce of water. In the case of 4 gm., two ounces of water were used. Aliquot portions were removed every 15 minutes for at least another hour for volumetric measurements, pH, free and total acid determinations.

*The formula of these tablets is indicated in Fig. 1.

Clinical:—Ninety-nine patients with ulcerative lesions and clinical symptoms of activity were treated with a bland diet and dihydroxy aluminum aminoacetate as an antacid (Table IV). The patients were instructed to chew two tablets (1 gm.) two hours after meals and at bedtime. Some patients with very active symptoms were given 1 gm. every two hours for 8 or 9 doses a day. This was especially true in cases of duodenal ulcer with partial pyloric obstruction and in the cases of gastric ulcer. No anticholinergic or antispasmodic or other drug was given except an occasional dose of phenobarbital as a sedative

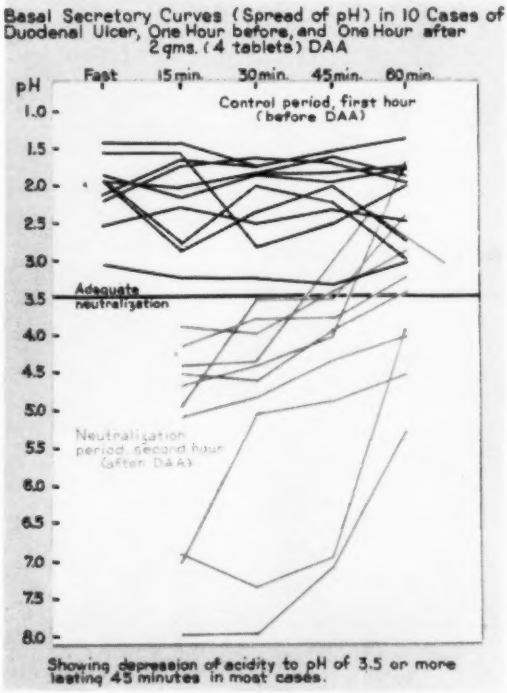

Fig 4

in a few cases. These patients were on treatment from three weeks to 1½ years. They were seen regularly by one of us—when hospitalized, daily; once a week until completely relieved; and every two or three weeks thereafter. A diligent attempt was made to determine whether the specific ulcer symptoms were relieved. Evidence of healing was grouped into clinical, x-ray, and gastroscopic categories.

Results

Diagnostic:—it is obvious from Table VII that the results were excellent, with dihydroxy aluminum aminoacetate therapy. The following x-ray and

gastroscopic serial views are illustrative of prompt and effective healing of peptic ulcers in our group of cases (Figs. 5a, b and c). Case L.S. was that of a middle-aged man who had a gastric ulcer on the lesser curvature with rather mild symptoms. He was treated sporadically over a period of months in the clinic before our study, with little evidence of healing, and was finally hospitalized for better control. The ulcer healed almost completely in 10 days, as observed by x-ray and gastroscopic control. Case A.D. was that of a 38-year old woman first seen with rather severe symptoms of partial pyloric obstruction due to healing duodenal ulcer. Eighteen months after subtotal gastric resection she developed a gastrojejunal ulcer. Although these lesions are often very difficult to treat medically, in this case healing was rather complete as shown by x-ray and gastroscopy (Figs. 6a and b). Case E.C. was that of a 40-year

TABLE IV

CLINICAL TREATMENT STUDIES WITH DIHYDROXY ALUMINUM AMINOACETATE IN 99 ULCERATIVE LESIONS

Method:—Only "active ulcer syndrome" cases used.

Ambulatory Rx—1 gm. (2 tabs.) chewed 2 hrs. P.C. & H.S.
Hospital Rx—1 gm. every 2 hours.
Bland diet, milk between meals.
Treatment periods—3 wks. to 1½ years.

Types of Cases:

Duodenal Ulcers	77
Gastric Ulcers	11
Gastrojejunal Ulcer	1
Malignant Gastric Ulcer (Early Surgery Refused)	1
Hypertrophic Gastritis	9
	99

old male who presented a fairly typical ulcer story and was reported by x-ray to have a benign prepyloric ulcer with some antral spasm. At gastroscopy the impression was that a malignant ulcer was present and surgery was advised. Surgery was refused so medical management was instituted rather intensively. Symptoms were relieved but never completely with bland diet and antacid therapy, nor did they disappear when anticholinergics were later addded (Figs. 7a and b). Gastroscopic views showed some evidence of healing and rough scarring but not the smooth epithelization of benign ulcer. Surgery was finally performed six months after diagnosis and carcinoma confirmed. No metastases were found.

Secretory:—Figure 2 is a graph of mean or composite secretory curves of pH and free acid in 30 cases with normal gastrointestinal tracts. Adequate suppression of free acid is indicated after introduction of dihydroxy aluminum amino-

TABLE V

CLINICAL RESULTS OF TREATMENT WITH DIHYDROXY ALUMINUM AMINOACETATE IN 99 ULCERATIVE LESIONS

	Cases	Completely Relieved			Not completely relieved
		Less than 1 week	1-2 weeks	3 weeks or more	
Duodenal Ulcer (Including 2 Partial Obstructions)	77	50	19	7	1
Gastric Ulcer	11	8	3	0	0
Hypertrophic Gastritis	9	6	3	0	0
Gastrojejunal Ulcer	1	1	0	0	0
Malignant Gastric Ulcer (Early surgery refused)	1	0	0	0	1
Total	99	65	25	7	2

acetate. (The unbroken lines represent pH. The broken lines indicate clinical units of free acid.) Figure 3 shows a similar graph of 20 duodenal ulcer cases indicating adequate suppression of free acid to a pH of 3.5 or above (or clinical units of approximately 0° free acid) for 45 minutes in most cases, after in-

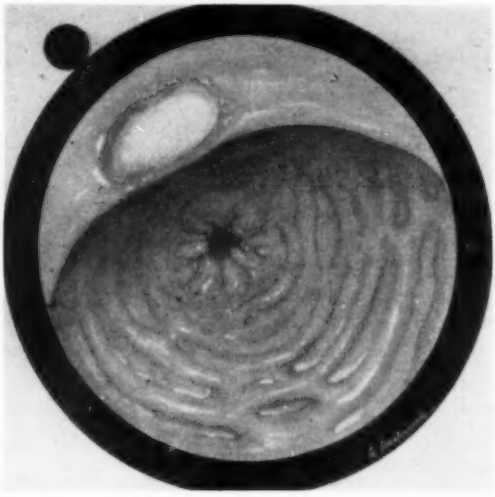

Fig. 5a—Case L.S., 9 February 1954. Benign gastric ulcer, lesser curvature. Serial gastroscopic views showing various stages of healing during DAA therapy.

troduction of DAA. If an antacid suppresses gastric acidity beyond pH 5 one is likely to get rebound or secondary rise of gastric acidity and perhaps some interference with protein digestion. Figure 4 shows the actual spread of pH in

TABLE VI

SUMMARY OF CLINICAL RESULTS
DAA THERAPY IN 99 ULCERATIVE LESIONS

Complete Relief of Ulcer Symptoms	99%
(Symptoms of "Irritable Bowel", Cholecystitis) (Other Associated Disorders—Not Relieved)	
Rapidity of Complete Relief—3 Days to 2 or 3 Weeks 90% Completely Relieved in 2 Weeks or Less	
Constipation Not Previously Noticed	3%
Nausea Attributed to Flavoring	1%

10 cases of duodenal ulcer before and after DAA. Volumetric suppression of gastric secretion was also noted after administration of DAA in some cases. This was not as uniformly consistent as suppression of acidity especially in the

Fig. 5b—Same case at Fig. 5a, 1 April 1954.

earlier experiments. Further observations are necessary for accurate elucidation of the volumetric phase.

Clinical:—Tables V and VI show that 90 per cent of the cases were completely relieved of symptoms in less than three weeks. Certain symptoms, such

TABLE VII

EVIDENCE OF HEALING IN 99 ULCERATIVE LESIONS
ON DAA THERAPY—3 WEEKS TO 1½ YEARS

		Complete or Partial Healing	Total Cases
Duodenal Ulcer	X-ray and Clinical Evidence	77	77
Gastric Ulcer	Gastroscopic Evidence	7	
	Clinical Evidence	11	
	X-ray Evidence	11	11
Gastrojejunal	Gastroscopic Evidence	1	
	Clinical Evidence	1	
	X-ray Evidence	1	1
Malignant Gastric Ulcer (Early surgery refused)	Gastroscopic Evidence	(Partial)	
	Clinical Evidence	(Partial)	
	X-ray Evidence	(Partial)	1
Hypertrophic Gastritis	Gastroscopic Evidence		
	Clinical Evidence	9	9
	X-ray Evidence		

as lower abdominal distress, bloating, aerophagy, might persist while the typical rhythmic epigastric burning or gnawing after meals would be effectively relieved. In some instances milder symptoms returned occasionally for longer periods. Only 7 per cent required periods longer than 3 weeks for complete

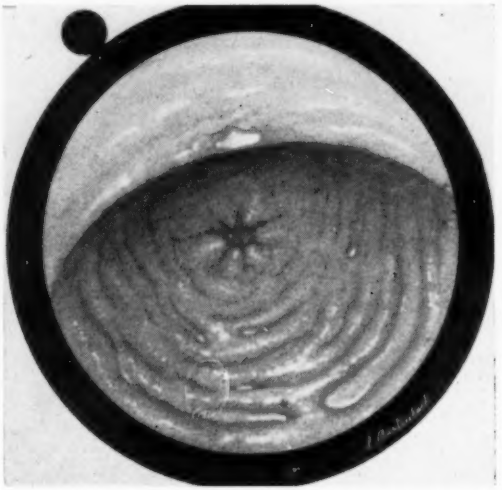

Fig. 5c—Same case at Fig. 5a, 9 April 1954.

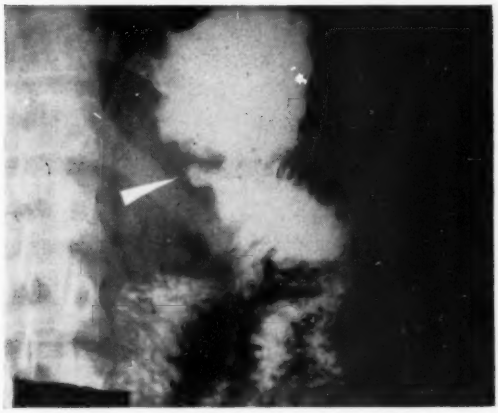

Fig. 6a—Case A.D., 8 June 1954. Gastrojejunal ulcer. Serial x-ray views showing stages of healing during DAA therapy.

relief and only 2 patients were in the category of not being completely relieved and one of these was a malignant gastric ulcer. Included is the interesting fact that only 3 per cent complained of constipation not previously noticed. One patient complained of nausea attributed to the peppermint flavoring of the

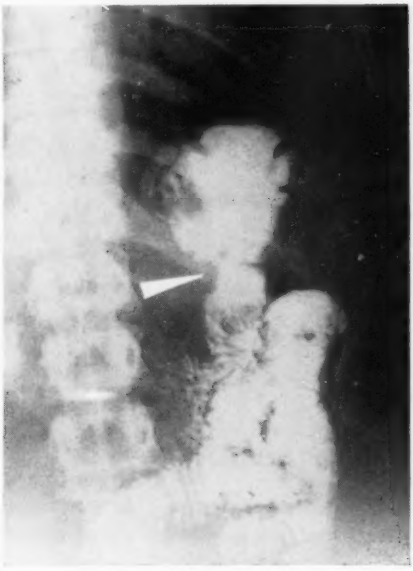

Fig. 6b—Same case as Fig. 6a.

drug. Two cases were not completely relieved. One of these was a case of malignant gastric ulcer which was not completely relieved even with very rigid management, including finally the addition of anticholinergics.

Comment

It is obvious from Figures 2, 3 and 4 that the drug selected, dihydroxy aluminum aminoacetate, is capable of suppressing gastric acidity to points within the range of the so-called ideal pH of 3.5 to 5 for an average of 45 minutes in most cases. Hollander calls this range of pH the point of proteolytic neutralization[7]. Suppression of gastric acidity to a pH of 6 to 8 is likely to be followed by a compensatory "rebound" of gastric acidity. As gastric acidity is reduced

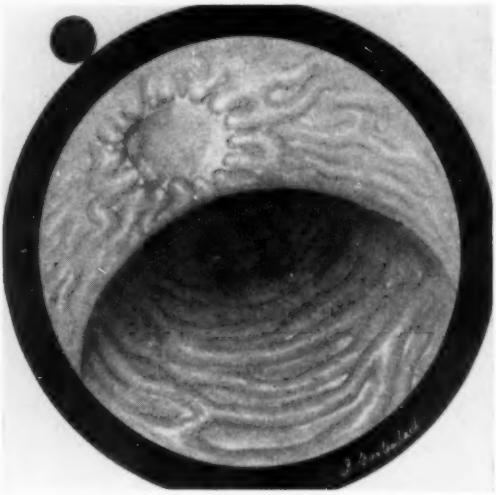

Fig. 7a—Case E.C., 5 October 1954. Malignant gastric ulcer, lesser curvature. Serial gastroscopic views showing stages of partial "healing" on DAA therapy (early surgery refused).

the digestive activity of pepsin is suppressed, and therein lies the efficacy of antacid therapy. The acid neutralizing power of the drug was just as effective in the stomachs with ulcerative lesions as it was in the 30 normal stomachs used as controls. Other experiments not detailed here involved secretory studies after histamine stimulation as well as in fasting basal secretions, with no essential difference in neutralizing effects.

As mentioned previously, our experience, as well as reports of other observers, indicates that the aluminum products are probably the most satisfactory antacids in use today. They are non-toxic, relatively unabsorbable, do not disturb acid-base balance, are capable in small quantities of depressing large

amounts of gastric acidity moderately but usually not below a pH of 3.5 to 5. Besides, they are said to have an adsorptive and an effective demulcent action. An important shortcoming of the aluminum products has been the marked tendency to produce constipation[8], especially when frequent administrations are desired. This occurs at times in spite of concurrent use of mild laxatives. In our treatment studies, dihydroxy aluminum aminoacetate was again used in preference to the aluminum hydroxides, hoping to avoid or to considerably reduce the complication of constipation, since this N.N.R. product contains 73 per cent less of the constipating aluminum element than the hydroxides[9].

Secondly, we sought to determine whether in other respects this aluminum salt of an amino acid should be regarded as an effective antacid, clinically.

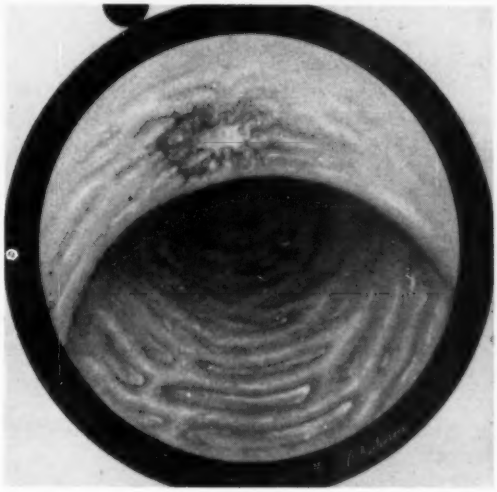

Fig. 7b—Same case as Fig. 7a, 15 December 1954.

All cases were treated with the aluminum product, dihydroxy aluminum aminoacetate (Robalate®) and bland diet. The approach was that of appraising and treating the total patient in addition to the local manifestation of disease. This included treatment and correction of associated organic disorders as well as evaluation and consideration of associated functional and psychogenic manifestations. This is important for complete and satisfactory relief of the patient's complaints, as well as for the prolongation of the period of remission from gastroduodenal ulcer. The incidence of recurrence of clinical symptoms after cessation of antacid therapy for one month or more was observed. All of these cases had originally been on regular treatment for three weeks or more before cessation. A correlation of anamnestic data indicated usually that recurrences were associated with short periods of therapy, or some

definite and specific episode such as dietary indiscretions, a bout of cocktails, acute upper respiratory infections, a period of prolonged emotional depression or anxiety, economic reverses, etc. There was x-ray and gastroscopic evidence of recurrence in one case of benign gastric ulcer of the lesser curvature 17 months after cessation of therapy. In all instances symptoms of recurrences were immediately alleviated by return to DAA treatment regime.

It is our feeling as in the case of E.C. with malignant ulceration, in spite of some reports in the literature to the contrary, that most cancerous gastric ulcers could be diagnosed by a careful analysis of the clinical course under rigid medical management over a period of four to five weeks. While this is not to be relied upon alone, it is an important adjuvant often equal to the laboratory methods in the differential diagnosis of malignant ulcer.

Summary and Conclusions

1. We have presented a report of 109 secretory studies which were made under fasting basal conditions or after histamine stimulation in 79 ulcerative lesions of the upper gastrointestinal tract, and 30 control cases with negative gastrointestinal tracts.

2. Free and total acidity and pH were electrometrically determined with a Beckman pH meter and volume of secretions was measured for 2 hours or more, before and after introduction of DAA into the stomach as an acid neutralizer.

3. Dihydroxy aluminum aminoacetate (Robalate®) was shown to suppress gastric acidity to a point within the "ideal" pH range of 3.5 to 5 for a period of 45 minutes in the majority of cases. These effects were produced in peptic ulcer as well as in the normal control cases after histamine stimulation and in basal gastric secretion.

4. Clinical response to treatment ran parallel to controlled gastric acid neutralization with DAA.

5. Clinical, x-ray and gastroscopic evaluation of response to therapy was made in 99 peptic ulcerative lesions in which DAA was used as an antacid.

6. There was excellent response in terms of relief of symptoms, clinical, x-ray and gastroscopic evidence of healing.

7. There were no significant side reactions and only 3 per cent of patients complained of constipation even with "around the clock" administration of the drug.

8. Incidence of recurrence of symptoms during 1½ years was found in most cases to be related to episodes of emotional strain, dietary indiscretions and intercurrent infections.

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PHARMACOLOGICAL BACKGROUND OF MODERN ANTICHOLINERGIC DRUGS*

KAO HWANG, M.D., Ph.D.

North Chicago, Ill.

In speaking of anticholinergic drugs I think we all know that the word "cholinergic" refers to the nervous mechanism mediated by acetylcholine in the central as well as the peripheral nervous system. Acetylcholine is released at the nerve terminals and acts on the effector cells. As shown in Figure 1, acetylcholine has at least two kinds of actions in the peripheral nervous system, namely, muscarinic and nicotinic. Muscarinic action occurs at the neuroeffector junctions of all postganglionic cholinergic fibers while nicotinic action takes place at the ganglionic synapses and the neuromuscular junctions. The anticholinergic drugs presumably compete with acetylcholine at the site of the effector cells. As a result, the action of acetylcholine is blocked, although it is still released at the

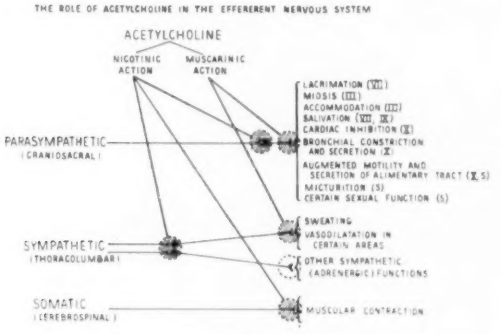

Fig. 1

terminals by the nerve impulses. This figure shows the sites of acetylcholine release and its physiological effects on various organs.

The anticholinergic action of a drug is attributed to the presence of a nitrogen atom as well as a blocking moiety in its chemical structure (Fig. 2). The nitrogen atom may exist in the form of either tertiary or quaternary ammonium. With the same blocking moiety, quaternization of the tertiary salt brings about marked changes in its pharmacological properties in the following general manner:

1. Greatly diminished effect on the central nervous system which effect is notorious with the tertiary salts.

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From the Department of Pharmacology, Abbott Laboratories, Chicago, Ill.

2. Greatly increased antimuscarinic or atropine-like activity.
3. Greatly increased ganglionic blocking and curare-like actions.
4. Greatly increased oral tolerance due to limited absorption.

The modern anticholinergic drugs we are going to discuss today will be restricted to a group of synthetic quaternary ammonium salts with potent antimuscarinic or atropine-like activity. Although the ganglionic blocking effect is markedly increased over their tertiary congeners and easily demonstrable in the laboratory animals, this effect requires many times the dosage which shows the

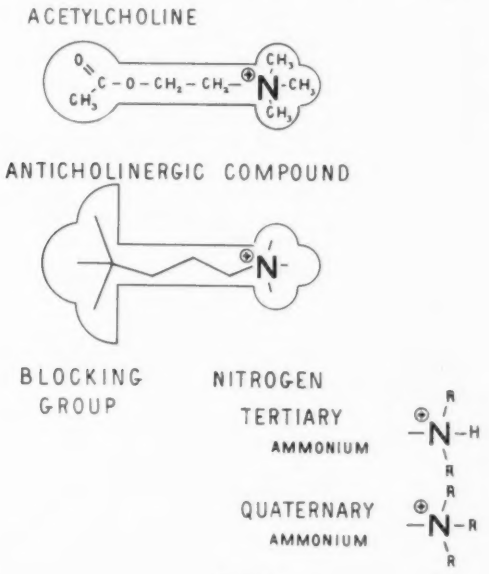


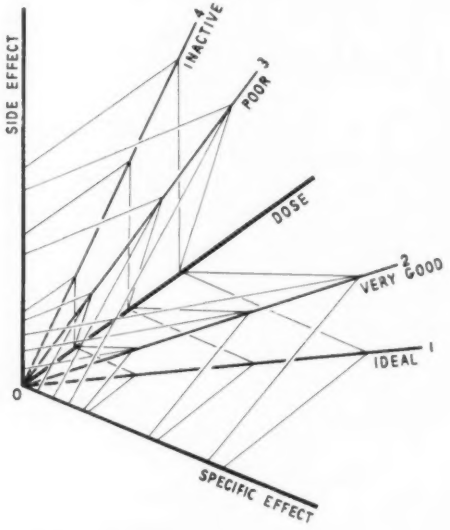
Fig. 2

antimuscarinic action. It is thus doubtful that ganglionic blocking effect can ever be achieved by the use of these drugs clinically without widespread undesirable side-effects. The curare-like activity of these drugs likewise requires very high doses. Therefore, the modern anticholinergics in the practical doses may be considered as purely antimuscarinic drugs, being similar to atropine but with little effect on the central nervous system.

Anticholinergic drugs are of particular interest to the gastroenterologist because of their alleged antispasmodic and gastric antisecretory effects based upon their antimuscarinic potency. In spite of the absence of toxicity on the central nervous system the main drawback of modern anticholinergics is the occurrence of various undesired and sometimes intolerable or harmful side-effects

which include dryness of the mouth and throat, blurring of vision, palpitation, urinary retention and others.

Theoretically these side-effects should always appear if all the cholinergic receptors in the various organs are equally blocked by the same dose. The facts that certain specific effect such as marked antimotility or antisecretory may be obtained with no or very slight side-effect and that one side-effect may appear in the absence of the others strongly indicate that the cholinergic receptors are not equally susceptible to the blocking effect of anticholinergic drugs. Thus, the anticholinergic drugs could possess a certain selective action on particular



A THREE DIMENSIONAL DIAGRAM OF THE DOSE RESPONSE RELATIONSHIP OF SEVERAL HYPOTHETICAL DRUGS

Fig. 3

cholinergic functions at relatively low doses. Higher doses would block more than one group of receptors and result in the occurrence of side-effects.

This selective action of certain anticholinergic drugs on the gastrointestinal tract apparently depends on the fitness of the chemical structure of the drugs to the configuration of the receptors. It is well known that slight changes of the chemical structure may alter a great deal of its potency and selectivity. There is no exact knowledge for the chemist or pharmacologist, on the basis of chemical structure or animal experimentation, to predict the clinical activity and especially such a desirable feature as being selective on the abnormal functions of the

gastrointestinal tract. Such a property can only be ascertained by careful testing in the human patient.

I would like to show you briefly some of our own experience on various synthetic quaternary ammonium anticholinergic compounds in Table I. The tests were made in different species of animals in comparison with atropine which is assigned an arbitrary potency of 3. Higher potency is expressed as

TABLE I

POTENCY OF DIFFERENT DRUGS BY VARIOUS METHODS OF ASSAY IN ANIMALS IN COMPARISON WITH GASTRIC ANTISECRETORY EFFECT IN MAN
(POTENCY GRADED 1 TO 5, ATROPINE = 3)

Tests (route of adm.) / Drug	Spasmolytic isolated rabbit ileum vs. ACh	Antisialogogue rabbit (I.V.)	Mydriasis cat (I.V.)	Tachycardia dog (I.V.)	Gastric antisecretory rat (I.V.)	Anti-ulcer Shay rat (Subcu.)	Gastric antisecretory basal secretion man (oral)*
Pamine (Upjohn)	4	5	–	5	–	5	5
ProBanthine (Searle)	4	3	4	–	–	5	5
Antrenyl (Ciba)	4	4	–	4	–	5	4
Tral (Abbott)	2	4	4	2	4	5	5
Atropine	3	3	3	3	3	3	3
Banthine (Searle)	4	3	3	3	3	5	3
Prantal (Schering)	2	1	2	2	1	3	3
AP396 (Abbott)	4	4	–	4	4	4	3
AP407 (Abbott)	3	2	3	2	1	3	4
AP478 (Abbott)	2	1	1	1	3	3	3

*Potency graded according to the results obtained in Dr. J. B. Kirsner's clinic (J.A.M.A., **151**:798, 1953, and personal communications).

4 or 5 and lower potency 2 or 1. Some compounds are less potent than atropine in some tests but more so in some others. The last column of this table represents the human data of their inhibitory effects after oral doses on the rate of basal secretion in persons secreting acid gastric juice continuously in moderate to large quantities. These were determined in Dr. Kirsner's clinic at the University of Chicago. The human effects are graded according to the drug's ability to produce anacidity and the degree of its side-effect. A drug

like the one at the bottom of the table apparently had some favorable indication of better gastric antisecretory effect in the animals but was a failure in the human test. The other compounds selected on the basis of general overall potent activity seem to have a better chance to be active against human gastric secretion with less side-effects. This may have illustrated an important point that data obtained from animals may give some lead but cannot be directly applied to humans.

What the gastroenterologists really want is an ideal drug which will produce the desired specific therapeutic effect but no side-effects over a wide range of dosage. Such a drug should be safe, orally effective and produce no tolerance on prolonged administration. I would like to show you another slide (Fig. 3) to illustrate some of these ideas.

The dose response curves of several hypothetical drugs are shown in a 3-dimensional diagram. You can see that there are axes for the dose, the specific therapeutic effect and the undesirable side-effect. Suppose both specific and side-effects are accurately measured and graded according to magnitude and duration. Number 1 in the figure would be the ideal drug which produces an increasing amount of specific effect with increasing doses without the appearance of side-effect. Number 2 is a very good drug which produces very little side-effect with increasing doses. Number 3 and 4 are very poor and inactive drugs which produce mainly side-effects. I can say that today we do not have an ideal or even a very good anticholinergic drug specific to gastrointestinal disorders. In the past few years, however, there has been a great deal of progress along this direction. This can be illustrated by the next figure (Fig. 4) with which I think you are all familiar. This mainly tells that potent antimuscarinic drugs in animals do not necessarily have gastric antisecretory effect in humans and that some drugs may be more effective and more selective than others.

Let us now examine how the gastric antisecretory effects may be achieved by the anticholinergic drugs. This, of course, requires a knowledge of the physiological mechanism that controls gastric secretion. Figure 5 will give you a bird's eye view of the current concepts concerning the various factors that stimulate gastric secretion. All the steps shown in this illustration are supported by evidence obtained mostly in animals but also a great deal from human beings although there are still some controversial points.

It is shown in this figure that the cholinergic nervous mechanism plays a very important role. The vagus nerve terminates in the ganglia of the Auerbach plexus at number 1. At numbers 2, 3, and 4 postganglionic cholinergic fibers stimulate the secretion of mucoprotein, pepsinogen and hydrochloric acid respectively.

Another important mechanism is the release of a hormone, gastrin, from the antrum to stimulate the parietal cells. Gastrin is apparently released partly

by a cholinergic mechanism through the vagus at number 5 in the illustration. But probably more important is its release by a mucosal cholinergic mechanism at number 6 when stimulated by secretagogues or by mechanical distention. The cholinergic vagal impulses and the gastrin potentiate each other in their stimulating effect on the parietal cells, and both probably stimulate the acid forming mechanism through the mediation of histamine.

Another phase of secretion of relatively less importance is the intestinal phase which stimulates the acid secretion also by a cholinergic mechanism at number 7. Besides, both peptic and parietal cells can be stimulated by adrenal cortical hormones independent of the vagal and gastrin mechanism.

It can be seen from this illustration that the cholinergic mechanism involved in the gastric secretion appears to be quite extensive. In order to block

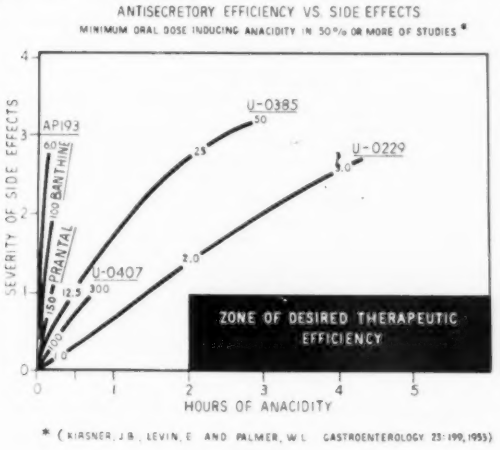


Fig. 4

the cholinergic function at number 1 in the figure, ganglionic blocking doses have to be used which are not practical. The cholinergic functions at numbers 2, 3, 4, and 5 can be blocked by the antimuscarinic action of anticholinergics at practical doses if these drugs are selective enough. The cholinergic function at number 6 is quite different from the others because it involves a cholinergic sensory receptor mechanism. It is stimulated or activated by secretagogues or mechanical distention of the antrum. It is however, very sensitive to the effect of antimuscarinic drugs in experimental animals. The cholinergic function for the intestinal phase of gastric secretion at site number 7 on the slide is less clearly understood regarding its mechanisms involved, but is apparently blocked by anticholinergic drugs.

If all the cholinergic functions as shown in the illustration from number 2 to number 7 could be blocked by anticholinergics, the control of gastric

secretion mediated through these channels would not be a problem. All these can be more or less achieved in the experimental animals by the use of anticholinergic drugs, but this accomplishment in the human patient is less certain.

Recent studies (Sun, Shay and Ciminera, 1955) have conclusively shown that as far as producing anacidity in fasting duodenal ulcer patients is concerned certain quaternary ammonium anticholinergic drugs are definitely superior to some others and also to atropine at the same level of side-effects. This is in support of the view that certain synthetic anticholinergics may have selective effect on the gastric secretory mechanism.

Another type of nervous stimulation is attained by giving insulin to produce pronounced hypoglycemia which stimulates the vagal centers through the hypothalamus. A complete block of this effect has been accomplished in animals with anticholinergics, but only partly so in human patients. In the

SCHEMATIC REPRESENTATION OF THE ROLE OF ACETYLCHOLINE IN THE STIMULATION OF GASTRIC SECRETION

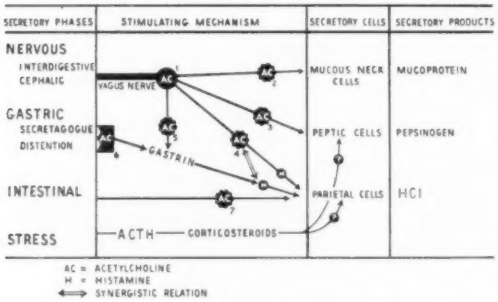


Fig. 5

latter species it appears that mucoprotein secretion is more easily blocked than the other secretions.

Regarding the gastrin release mechanism in humans only very limited studies were made with the modern anticholinergics in the peptic ulcer patients. The results seem to indicate that the response to a meal may be greatly diminished by the use of a certain anticholinergic drug, but apparently rather high doses may be required.

The difficulties experienced in blocking the response to the insulin hypoglycemia and the response to the test meal in the ulcer patients do not necessarily mean that the mechanisms involved are noncholinergic. More efforts should be made to have more drugs tested in order to find a more specific or selective anticholinergic.

When a potent and selective anticholinergic becomes available, its expected pharmacological effect on the gastric secretion might prove to be equivalent to a postganglionic vagotomy plus resection of the antrum.

Another aspect of the therapeutic use of anticholinergic drugs is their antimotility action. The mechanism of the gastrointestinal motility is mainly cholinergic. Although some noncholinergic mechanisms have also been described, their exact role in the gastrointestinal hypermotility is not clearly understood. Many anticholinergic drugs have been shown to be effective in suppressing the gastrointestinal motility in experimental animals and human patients. Here again the drug should be highly selective in relieving hypermotility or spasm and yet should not completely paralyze the transport function of the digestive tract.

One important general principle should always be borne in mind—that is, the anticholinergic drugs, when given orally, become effective only after being absorbed. There is a barrier in the intestinal tract that prevents the quaternary ammonium salt from being absorbed efficiently. This may partly account for the tremendous individual variations in the oral dosages for any of such drugs to produce the desired effect.

To summarize, the modern anticholinergic drugs are mainly quaternary ammonium salts which have a marked antimuscarinic activity. These drugs may show some selective effect in antagonizing certain exaggerated gastrointestinal functions. Although the ideal drug has not been discovered, judicious use of the available drugs may be associated with only relatively mild side-effects. The orally effective dose should be individually titrated.

It may be stated that the use of anticholinergic drugs is a sound approach to attack the pathophysiological mechanisms involved in the gastrointestinal disorders. It must be realized, however, that there may be mechanisms other than those being cholinergic that actually contribute to the particular disorder. In addition, the response of a patient to a drug may sometimes be attributed to factors other than the expected pharmacologic actions. Therefore the factors responsible for the pathogenesis of the particular dysfunction and those for the therapeutic response are both variable and multiple. Reliance on anticholinergics alone, even when an ideal one is available, will not solve all the therapeutic problems. This type of drug, however, is definitely valuable in the management of various disorders of the gastrointestinal tract, but the interpretation of the result should be very careful.

PEPTIC ULCER: MEDICAL CURE BY AN AMBULATORY REGIMEN*

N. E. ROSSETT, M.D., F.A.C.P., F.A.C.G.

Memphis, Tenn.

Introduction

A regimen for the hospitalized patient with peptic ulceration which produced verified gastric "free achlorhydria" (pH of 3.0 or higher) has previously been reported[1]. This regimen utilized a mixture of four parts aluminum hydroxide gel (U.S.P.) and one part by volume of milk of magnesia (U.S.P.) as the antacid. The anticholinergic agents used were tincture of belladonna in 1,288 patients and Banthine® in 146 patients.

This report presents the results of the same regimen with ambulatory patients and levorotary hyoscyamine† as the anticholinergic agent.

Regimen

Antacid:—A reactive mixture of 4 parts of aluminum hydroxide gel (U.S.P.) and 1 part of milk of magnesia (U.S.P.) prepared by a local pharmacist was used by most of the patients. The dose was one ounce between meals, upon retiring to sleep, 12 o'clock midnight and 2 A.M.

Anticholinergic drug:—The anticholinergic agent used was l-hyoscyamine sulfate. The dose was usually 0.25 gm. 30 minutes before meals and 0.5 mg. upon retiring to sleep.

Dietary:—A convalescent ulcer diet was started on the first day of therapy. This diet is described in full detail in another publication[2].

Supplemental doses of 50 mg. of ascorbic acid were given with breakfast.

Education:—Each patient was interviewed personally before being placed on therapy. Patients were permitted to see their x-ray films. About a half-hour was usually devoted to explanation of what the regimen, diet, antacid and anticholinergic agent were designed to do. A manual covering these facts was given to each patient as reinforcement.

Selection of Patients

Consecutive patients with radiographically verified duodenal deformity, niche, or both, and gastric niche seen in private practice were selected. The majority had been on various other regimens, usually with greatly restricted

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†Supplied as scored tablets containing 0.25 mg. l-hyoscyamine sulfate by Kremers-Urban Company, Milwaukee, Wisc. Their trademark is Levsin Sulfate.

diets and irregular schedules of antacids and anticholinergic agents. Relief of pain, let alone ulcer healing, had not occurred. An attempt was made to secure compression films as a follow-up in one to four weeks. The group consisted of 122 males and 20 females, a total of 142 patients. The average age was 44 years with a range of 18 to 78 years. The average duration of the ulcer history was 8 years with a range of 1 week to 31 years. About 67 per cent of the patients had an ulcer history of 4 years or more. The number, percentage, and location of the ulcers were shown in Table I.

TABLE I

	Males	Females	Total	Percentage
Duodenal	114	18	132	93 %
Gastric	5	1	6	4.2%
Jejunal	1	1	2	1.4%
Gastric and Duodenal	2	0	2	1.4%

In the 142 patients there were 148 episodes of ulceration.

Results

Prompt disappearance (within 24 hours) of pain was experienced by all except 4 patients. Of the latter, two had complete disappearance of pain by the second, one by the sixth and one by the seventh day.

TABLE II

Time Required to Become Pain-free

Days	Duodenal	Jejunal	Gastric	Duodenal and Gastric	Total
1	133	0	6	2	141
2	1	1	0	0	2
6	1	0	0	0	1
7	1	0	0	0	1
	136	1	6	2	145

No pain data on three patients.

These results in ambulatory patients with l-hyoscyamine sulfate are superior to our results in hospitalized patients using tincture of belladonna or Banthine[1].

In all but two, at least compression filming using a Scholz filming fluoroscope was done from one to four weeks after the start of therapy. All showed niche healing (when a niche was demonstrable) to the point of radiographic disappearance except for two patients. One, R.C., a 48-year old male with a postbulbar crater had prompt relief but failed to return for regular follow-up films. He was seen one year later, asymptomatic, with only scarring at the previous point of ulceration. The other, A.B., a 34-year old attorney, had pain relief in 7 days but failed to return for any follow-up. By telephone follow-up he claims to be asymptomatic.

Table III shows the results in the ambulatory group of patients.

TABLE III

TIME REQUIRED FOR CRATER-HEALING

Weeks	Duodenal	Gastric
1	2	1
2	85	4
3	4	1
4	7	1

Compared to the hospitalized group of patients at a Veterans Hospital previously reported[1], the results were at least equal for niche healing. In that series, duodenal niches had an average healing time of 2.16 weeks or 15 days with a range of one to 6 weeks. In the ambulatory group, duodenal ulcers had an average healing time of 2.14 weeks or 15 days with a range of one to four weeks. The average healing time for hospitalized patients with a gastric crater was 2.41 weeks or 16.9 days with a range of one to five weeks, compared with our ambulatory group with an average healing time of 2.3 weeks or 16.1 days with a range of one to four weeks.

Side-effects with doses of 0.25 mg. of l-hyoscyamine were negligible. Of the 142 patients, one female patient, age 77, complained of dry face and stumbling; another female patient, age 42, complained of blurred vision; and a third patient, male age 50, complained of slight hesitancy and frequency in urination. In doses of 0.5 mg. there was some drying of the mouth, especially in small people, but the effect was not severe enough to provoke complaints or reduction of dosage. In this study on ambulatory patients we were not able to do motility studies, but it appears that l-hyoscyamine has less effect on normal gastric motility as evidenced by its successful use in patients having gastric obstruction.

It has less constipating effect than Banthine and some of the other synthetic antispasmodics. Three male patients have been on l-hyoscyamine sulfate for periods ranging from 2 to 4 years because of previous frequent pain or hemorrhage recurrence. They have remained asymptomatic and no toxic manifestations have occurred.

Comment

We believe we have already demonstrated that all uncomplicated peptic ulcerations can be healed in the hospitalized patient[1]. It was the purpose of this study to see whether this could be achieved in the ambulatory patient permitted to continue his or her usual pursuits. This relatively small series indicates uncomplicated peptic ulceration can invariably be healed by the production or near production of "free achlorhydria" in the ambulatory patient and in remarkably equal time. Because of our favorable experience with large doses of tincture of belladonna and atropine as anticholinergic agents, we decided to use the levorotatory isomer of atropine, levo-hyoscyamine or l-hyoscyamine. Atropine is a racemic mixture consisting of equal amounts of the two optically active isomeric compounds, l-hyoscyamine and d-hyoscyamine. L-hyoscyamine occurs naturally in plants of the belladonna, stramonium and hyoscyamous families. If care is not exercised in extracting it, most or all of it may be racemized and converted into atropine. Commercial atropine is usually manufactured by racemizing l-hyoscyamine in an alkaline solution. Atropine *per se* probably does not occur in the plant. There is good evidence that the antispasmodic activity and other peripheral effects of atropine are due to the presence of l-hyoscyamine[3-9]. The intestinal effects of l-hyoscyamine have been studied by Exler and Van Niekerk[7], Von Cettingen and Marshall[8], and Levy[9]. These reports indicate that l-hyoscyamine is approximately twice as active as atropine. Recently Ward et al[10] studied the antispasmodic activity of 5 drugs by means of parallel tests on the isolated guinea pig ileum, and by the inhibition of intestinal motility in the intact rat.

Comparisons on a dosage basis indicate that l-hyoscyamine hydrobromide is approximately twice as potent as atropine sulfate, and that atropine has about 10 times the potency of homatropine methylbromide and 250 times the potency or Trasentine®. Banthine, which was found to be approximately equipotent when compared to atropine sulfate on the isolated ileum, appeared about half as potent in the intact rat. Pharmacologic studies indicate that l-hyoscyamine on a dose basis is the most potent anticholinergic agent available. There is evidence that the dextro isomer, d-hyoscyamine, contributes to the central effects of atropine[1,11,12,13]. Ward et al[14] have shown that the cholinergic blocking effect of the l-isomer contained in atropine appears to be diminished by the presence of the d-isomer under certain experimental conditions.

As supplied commercially l-hyoscyamine sulfate contains variable and substantial amounts of d-hyoscyamine. L-hyoscyamine is pure l-hyoscyamine sulfate,

from which the d-isomer has been removed. We used Pamine® in 11 ambulatory patients and Pro-Banthine® in one ambulatory patient to date. These are not included in the group of patients reported in this paper. Our experience in hospitalized patients includes Monodral®, Tricoloid® and Centrine®. We can find no particular advantage offered by the synthetic antispasmodics.

Conclusions

1. L-hyoscyamine, the levorotary isomer of atropine proved to be an effective clinical anticholinergic agent when administered in doses of 0.25 mg. 30 minutes before meals and 0.5 mg. upon retiring. At this dosage level, side-effects were negligible.

2. Prompt disappearance of pain on the first day occurred in 141 of 145 ulcer episodes occurring in 142 patients.

3. The regimen previously described and used in the hospitalized patient[1] will without exception heal the uncomplicated ulcer in the ambulatory patient in equal time.

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Discussion

Dr. I. Snapper (Brooklyn, N. Y.):—Most of the ulcer patients who come to us can be cured—at least temporarily—with many different diets, and many different medicaments. All of you who were here last year, heard Dr. Gray discuss how ACTH increases the peptic acidity of the stomach juice. If we can impress our patients sufficiently, if we can restore their mental balance, then the ACTH secretion will decrease and the stomach will come to rest.

If I had an ulcerating stomach and went to Dr. Rossett or Dr. Berry, my ulcer would do well, irrespective of the treatment they would prescribe, because my confidence in either of them would decrease my ACTH production.

We, therefore, encounter a very large group of ulcers who progress satisfactorily under influence of our therapeutic ministrations. Unfortunately, there is a smaller group of ulcer patients who do not do well, irrespective of our diets, medicaments, persuasions and rationalizations. These patients we ultimately entrust to the hands of Dr. Wangensteen and his colleagues.

We hope, however, that thanks to the work of the men we have heard today, and their colleagues all over the world, one day the solution will be found, which will permit us to cure all peptic ulcers without surgery. Perhaps Dr. Hwang will succeed in finding an all inclusive anticholinergic drug without the disagreeable side actions about which our patients complain so frequently.

One cannot discuss indiscriminately medical treatment of ulcer of the stomach and of ulcer of the duodenum. Every ulcer of the stomach should be looked at askance because of the possibility of malignant degeneration. We can play with drugs and diets in duodenal ulcers; we should not play too much and too long with them in the treatment of gastric ulcers.

Dr. C. W. Wirts:—If time permitted I would like to ask Dr. Wangensteen what his present feeling is as regards the position of the pendulum. Certainly it was not long ago that one found in the literature, medical as well as surgical, that all aspects of gastric defects should be looked upon with sufficient suspicion that surgical intervention be considered.

Recently, at least in medical circles, as a result of rather well documented cases studied at the Lahey Clinic under the auspices of Dr. Smith and Dr. Sara Jordan and, more recently as a result of a report of over 200 cases with good follow-up from New Orleans, studied by Dr. Donovan Browne, we have been inclined to feel that surgery is not mandatory in all cases of gastric ulcer. With adequate supervision in the diagnosis of these cases, using all means available, those requiring surgery should be able to be separated from those that do not.

Of course it is assumed that these patients are carefully followed to complete healing of the lesion.

Dr. Owen H. Wangensteen (*Minneapolis, Minn.*):—I am not certain I can say anything very helpful in this discussion. I have listened with pleasure and some profit, I hope.

The question of mortality of peptic ulcer never seems to affect discussions like this. Yet, in the final analysis, it lies at the very heart of the problem. Dr. Berry, I believe, talked about healing over a period of observation of one to three weeks. The present is important to all of us but the future also is of some importance to most of us. I think it would be profitable and pertinent to this discussion if Dr. Berry, in looking back over an experience of five years, would tell us how many of these patients which he cured with this drug, have died of their ulcer, or still have their ulcer after a period of five years.

Dr. Rossett takes us back to the period of 1940, since which period of time he has been (using his own words) studying this problem very intensively. I would like to ask him the same question. What of those patients now? How many have died of ulcer? How many still have their ulcer?

We know of internists all over the world, who have a keen interest in the problem of peptic ulcer and who have been keen over conservative treatment, who have come to the realization that ulcer is a continuing disorder, and something more effective than words or milk is necessary to effect a cure.

Arthur Bloomfield, who has written books upon the subject, has within the last year [Emile Holman Festschrift, Am. J. Surg., **89**:1109, (June), 1955] capitulated and said that any ulcer which is resistant to medical management over a short period of weeks he sends to the surgeon for surgical relief, because of the high incidence of recurrence, and mortality from hemorrhage.

Krarup, one of Meulengracht's associates at the Bisbebjerg Hospital in Copenhagen, said as much nine years ago and stated that patients were being referred to surgery on lesser indication than previously because of the failure of medical management to thwart ulcer recurrence. Internists all over the world, are capitulating to this thesis: Walther at Vienna, Römcke in Scandinavia, and others in our own midst. Yet, I have heard a prominent gastroenterologist within the past year insist that he would not have a patient of his with an ulcer see a surgeon unless there was no other way out. It would be good to know something of that internist's cases. What blindness in his vision!

We might as well look at the problem realistically because we are all interested in observations that extend beyond a short period of time. Certainly, much has been said in this discussion that could be of help and great interest to the patient with an ulcer. The longer view, however, is what counts.

During the past summer, I spent some very interesting, enjoyable and profitable days reading over some of the papers of the old Russian school. I used to think those papers were published in Russian because they were published in the Russian Journal of Physiology, but most of them are in French. If you have not read some of the classical papers of the Russian Pavlov School in this Journal, I would urge you to do so. Many have a very, very modern ring and have important pertinence to the problem of ulcer today.

For instance, in the standard medical management of ulcer, meat is decried. Long years ago, Lobassow showed there are more extractives in fish than in ordinary beef. He did show too in the isolated gastric pouch of the dog that broiled foods, in which the surface of the fish or meat is superheated—that this mode of preparation pyramids the acid secretory effect of both meat and fish. Yet, standard diets employed by dietitians and gastroenterologists often suggest that fish can be eaten when beef should not.

Large quantities of meat, I am certain, should be denied the patient on a dietary ulcer regimen, as should also coffee, tobacco and alcohol—especially beer. These considerations, however, are essentially outside of the range of my present purview.

Certainly, I would like to emphasize the word of caution Dr. Snapper alluded to in the management of gastric ulcer. Certainly, many of these gastric ulcers which are being cured by medical management turn out to be cancer. I do not know exactly how high the percentage is, but it is high enough to label the method as unsafe without the most careful scrutiny and review by a competent gastric surgeon.

As I came in here this morning, I picked up a copy of the October 1955 issue of The American Journal of Gastroenterology. You will find it interesting reading, I know. The panel on gastric ulcer and cancer shows a wide divergence of opinion, which is always manifest in these discussions. I believe the majority of observers who follow up a group of gastric ulcers for a long period of time will find many gastric cancers in such groups.

I would particularly allude to the circumstance of the limitation of the roentgenologist's capacity to interpret these lesions, particularly antral lesions. If a patient comes from a radiologist with six films, and five show defects and the sixth doesn't, one is inclined to say that it is spasm. But in that category of situations, I am beginning to find there are some cancers. I believe the roentgenologist is going to improve his ability to interpret lesions as he concerns himself more with just such differences. You like to have all six films show the defect, but sometimes those five positive films suggest that the patient may have a small, superficial spreading cancer of the antrum. I therefore put great stress on the presence of achlorhydria. Unfortunately, it is not a uniform finding. Any

patient who has a gastric defect and has achlorhydria, should be looked upon as having a gastric cancer.

Some of you are probably familiar with the work of Professor Komei Nakayama of Chiba City, Japan, who uses radioactive phosphorus in the detection of cancers of the esophagus and stomach. On his last visit here (Sept. 1955) Nakayama demonstrated this technic in our clinic. He gives the radioactive phosphorus 48 hours before he puts down a Geiger counter on the tip of a long flexible bougie. An increase in counts of 2 to 3 times over the normal suggests the presence of a malignancy. We have recently had an 83-year old lady who is achlorhydric and has upper abdominal pain. Roentgenologically she was negative. There was some question of a lesion in the antrum on gastroscopy. This technic may prove to be very useful for the surgeon as well as the pathologist in differentiating benign and malignant gastric ulcer.

My Surgical Resident, Dr. Alan Thal, operated upon this lady, and removed a goodly segment of her stomach. Frankly, there was little or nothing to see. When the stomach was taken out, Drs. Donald Shahon and Joseph Aust went over it with a Geiger counter. There was 100 per cent difference in concentration in a small area in the antrum. That area then was carefully studied. There was a carcinoma *in situ*. The stomach was put in the ice-box and exposed to an x-ray film over a 48-hour period. The heavy dark spot on the radio-autograph was sectioned; it was a microscopic cancer!

Our critics said, "She is 83. What have you done?" I am not certain what we have done. I hope we have made her happier. There are considerations beyond that, however. She got rid of the pain immediately. I do not know how long a woman of 83 will yet live. But some such patients are 50, and that is why the matter is of such great importance.

Additionally, I would like to say that one must look upon healing of a gastric ulcer as *sine qua non* evidence of cure, because a well regulated medical regimen will heal out a superficial spreading cancer; I have seen that happen.

As Dr. Snapper has said, gastric ulcer and duodenal ulcer are probably different diseases. From studies which have been published by others, and from studies now under way in our clinic, it would appear that the ultimate cause of duodenal ulcer is the gastric juice itself. In gastric ulcer, however, it is probably the increased vulnerability of the gastric mucosa to be injured by a juice of rather low digestive power which is responsible for the ulcer.

If one aspirates gastric juice from patients who have duodenal ulcer and drips it onto the cat's esophagus, perforation occurs frequently—not so with the gastric juice from patients with gastric ulcer. We are extending this technic to a study of the effectiveness of various kinds of operations. Preliminary studies suggest that a segmental resection probably comes nearest meeting the requirements of the ideal operation for duodenal ulcer.

The important cause of mortality in ulcer is hemorrhage. Until one has better methods of dealing with it, I think the surgeon is going to continue to have an important place in the management of peptic ulcer.

I hope that this conference will not break up without some of our speakers who have participated in this program telling us quite frankly that they did not succeed in curing their patients permanently with the regimens which they have extolled to us.

Dr. Wirts:—Thank you, Dr. Wangensteen. I think it would be valuable if we could have a rebuttal or concluding statement from the preceding speakers, particularly as to the results of recurrences and long-range follow-up. I think we could take a few minutes for that.

Dr. Berry, would you like to start off?

Dr. Leonidas H. Berry (Chicago, Ill.):—I would like to say I am glad Dr. Wangensteen emphasized the fact of the importance of recurrence. I think we all agree there is no great trick to supervise or preside over the healing of an ulcer. Recurrence is really the great problem.

In our cases, as far as we could see, we had as many recurrences within the year and one-half of our observation as anyone else.

In reference to the patient that we treated for a period of three months with malignant gastric ulcer, I want to say that he finally agreed to surgery, and had his resection. Now it has been about seven months, and he is doing fine.

Dr. N. E. Rossett (Memphis, Tenn.):—Dr. Snapper perhaps will recall that approximately six years ago we discussed this very thing at the University Club in Memphis, Tenn. We agreed that the metabolism of calcium and phosphorus, might be involved, and that investigative fields in this direction are wide open.

I also brought out the fact at that time that my original training was with John Peters of New Haven, and he was strictly a non-antacid man. It was this sort of training with no results in the outpatient department and wards that made me accept a research fellowship at Cornell in 1940.

I am quite delighted with the fact, at least until the ultimate cause of peptic ulceration is discovered, that our method was one way of relieving the patient of pain, and healing his peptic ulceration promptly.

I think research should continue, and the versatile mind of Dr. Snapper probably can offer a hundred directions in which the research should travel.

We have found the uncomplicated ulcer, including the ulcer of hyperparathyroidism amenable to therapy. I would love to take a crack at some of the refractory cases, so-called, Dr. Snapper has on his wards, and which he sees in the hospital.

Our experience in the Army and in the Veterans Administration Hospitals was entirely with a group of so-called refractory patients that were sent to us from an eight-state area. Either the patient or the physician was refractory, not the ulcer.

It will take many more years to tell about our recurrence rates. So far it appears that about 30 per cent of our patients will not have recurrence, going on with the diet you saw, having learned about how to live with their disease during their hospital stay or while ambulatory.

There have been no refractory ulcers in the uncomplicated group. Our mortality rate is zero in this group. Our mortality rate in the bleeding group, uncorrected, is 1.6 per cent. Indeed, a colleague of Dr. Wangensteen's, Dr. Mike Bowers first came to our hospital at Memphis, fully assured that bleeding ulcers ought to be operated on and, all gastric ulcers ought to be resected because of the possibility of malignancy. The total number of gastric ulcers on which we passed and said were benign was almost 200. As yet (4 years later) we have not had one come back that Mike Bowers could say "this was a malignancy you thought was benign". But it took infinite pains and the use of compression filming continuously and the gastroscope. The arrangement we had with Dr. Bowers was operation if we could not show definite healing to half size or better in two weeks in his gastric ulcer patients. In the vast majority of the cases that were benign, this occurred. Dr. Bowers is now the exponent of conservative medical management in bleeding ulceration.

I think Dr. Berry could raise his batting average from 90 to 100 per cent, if he will merely add an anticholinergic agent to his regimen.

The anticholinergic agents were not used with Pavlov's conditioned response experiments.

A REVIEW OF GROUP THERAPY IN WEIGHT REDUCTION*

S. WILLIAM KALB, M.D., F.A.C.G.

Newark, N. J.

The use of group approach to weight reduction is becoming popular in many communities throughout the country. Classes have been and are being organized by medical and nonmedical groups. We are particularly concerned with the weight reducing classes similar to those which are being held under the auspices of the Essex County Medical Society and the Essex County Heart Association in Newark, N. J.

Our first group was held at Saint Michael's Hospital and since then we have been holding classes in the adult schools and in other hospitals.

In order for any member to participate in a group they must have a certificate from their family physician admitting them to the group. Classes are held two hours weekly for 10 to 15 weeks.

The leaders of the group consist of an internist, psychiatrist, nutritionist or dietitian and social service worker. While the patient comes to a weight reducing group primarily to lose weight, she is given psychiatric guidance and/or treatment. Psychiatric testing reveals the personality of the obese as she thinks she looks to herself and how she imagines others see her. Her attitude towards her family and her friends is brought out into the open.

The first lecture is more of a social get-together and at this time a summary of the programs which are to follow is outlined. Each patient in the group becomes familiar with the others and with the leaders of the group. This gives them a common ground for participation and a sense of belonging. Everyone seems to be "in the same boat" so that no feeling of being dominated exists. Hence, there is less resistance and the desire to follow the leader becomes evident. They learn what to expect and what not to expect. They know they have a definite time to accomplish a certain amount of weight loss. It is important that they should have a similar age level, social level and economic status[1]. In this way they feel that they are all equal. Weight reduction helps to overcome the feeling of inadequacy and any inferiority complex that may exist.

The leaders must be well informed on the subject of foods, food habits and group psychotherapy. They must have a sympathetic understanding of the problems which are brought out during these meetings and demonstrations. The groups are limited to 15 in number. If more are taken, the group becomes unwieldly and too much time is spent in repetition.

*Read before the Second Annual Convention of the American College of Gastroenterology, Chicago, Ill., 24, 25, 26 October 1955.

It is essential that the patients have a complete physical and laboratory examination before they enter the class. The laboratory examination should include a basal metabolic rate determination, urinalysis, hemoglobin, blood sugar, cholesterol and electrocardiograph. Reports are issued at the end of four weeks to the referring physician. These tests are done in order to determine if any other pathology is present which is not connected with the obesity. A review of the literature[2,4] on obesity failed to reveal any intrinsic metabolic, endocrinologic or central nervous system abnormality in the average case.

The psychologic causes of obesity are gaining greater recognition today[5]. These are divided into two subdivisions: one is obesity without serious emotional disturbances and the other, obesity with serious emotional disturbance.

The sessions are informal and the members are allowed to ramble on about any subject that interests them. Most of the grievances, however, are about their home life. There seemed to be a misunderstanding with their parents or their mates.

The patients are placed on a low fat, low carbohydrate diet. The diet which was used is as follows:

FOODS ALLOWED DAILY

Milk	One pint. Skim or buttermilk.
Eggs	Three times a week. 2 eggs may be substituted for meat at the meal.
Meat or Fish	¼ pound lean meat or fresh fish. Boiled, broiled, roasted. *No gravy.*
Vegetables	As desired: Asparagus, stringbeans, broccoli, cabbage, carrots, cauliflower, celery, chicory, cucumbers, escarole, eggplant, lettuce, radishes, spinach, squash, tomatos, tomato juice, turnips.
Fresh Fruit in Season	One portion of: Blackberries, grapefruit, melon, orange, peach, pineapple, raspberries, strawberries.
Beverages	Two cups: Coffee, tea, Postum, Sanka.

Use a little salt in the preparation of the food. Add none after serving.

THIS DIET MAY BE ARRANGED AS FOLLOWS

Breakfast	*Lunch*	*Dinner*
Fresh fruit—1 portion Skim milk—1 cup or beverage—1 cup	Salad—(egg, salmon or tuna fish or two eggs) or cottage or pot cheese, skim milk or buttermilk, beverage.	Meat or fish—¼ lb. Vegetables and salad from list as desired. Skim milk—1 cup. or buttermilk—1 cup or beverage—1 cup.

The diet can be made flexible to meet the individual requirements from 900 to 1,500 calories.

The average weight loss in our series amounted to two pounds per patient per week. Two per cent of the members failed to lose the estimated amount as set forth in the beginning of the program.

No medication was given. Nearly all of these patients had been on diets before and have had amphetamine in one form or another. Because these were all referred patients we did not want to complicate our treatment by subjecting them to any side-effects caused by medications[6,7]. This does not necessarily mean that we do not endorse anhedonic drugs.

Environmental factors, such as parents being hypercritical, belittling and too demanding contributed in large measures to the obesity.

Obesity to many of these patients is an outward manifestation of good strength. They feel that this heavy layer of fat is a protective covering for them against such diseases as tuberculosis and cancer.

At the Herrick Memorial Hospital in Berkeley, Calif.[1], a review was made of 100 cases that were treated by group therapy. Personality tests were evaluated for each patient. One test revealed psychosomatic, depressed neurotic, hysteric, schizoid personality and other diagnostic categories. Another test showed how one interacts with others. The problem of an overweight person was as diversified in this group as in any other group. Clinical observations, however, showed many similarities such as overeating, lack of exercise and always being on some kind of reducing diet, but not sticking to it very long.

There is a sense of independence and resistiveness in obese women who come to the physician's office to reduce. They have an attitude of "I dare you to help me" instead of a submissive attitude of one seeking out help. The patient is not quite sure of her own emotions. She would like to have a cute figure and be in a position to take one or two sizes smaller in her clothes but she refuses to be dominated or restricted to a limited amount of food. When this same patient becomes part of a group the problem of weight reduction resolves itself differently. This difference[8] occurs in the following manner:

a. The opportunity the members have to talk and listen to others having the same problem, the same goal and the same diet put them in a cooperative position.

b. The group exerts a competitive influence.

c. They develop a better understanding of themselves.

d. The way in which the group helped individuals with family or personal problems. This pooling of the experiences and knowledge of the members produces a type of assistance that is meaningful to the individual concerned.

e. Listening to several authorities on the same subject from different viewpoints gives her a feeling of authenticity.

f. Food demonstrations, food substitutions, and an exchange of ideas on preparing low calorie recipes makes her better equipped to handle a diet.

Many feel that weight reducing should be done by the psychiatrist rather than by the internist or the general practitioner. This has not worked out too well except for a small minority who had a need for psychiatric therapy apart from the obesity. I have had patients who received psychiatric treatments for as long as five years and in most instances, the obesity is still with them.

The pattern of eating in the obese patient shows that most of them never eat breakfast and some just drink coffee. Nearly every one of them consumes a caloric intake of some 200 to 4,000 calories between their dinner at night and bed time. These television snicks and midnight snacks are in addition to their basic caloric intake and are often blamed on "hunger pains".

It is apparent that the sensations from the stomach and duodenum are important[9]. Intensive stimuli from the "empty" gastrointestinal tract are interpreted by the central nervous system as "hunger pangs". The stomach, however, has not an autonomous role as indicated by the fact that its removal does not abolish feeding behavior. Grossman, Cummins, and Ivy[10] have demonstrated that a complete denervation of the upper gastrointestinal tract does not greatly impair the dog's ability to regulate food intake.

Exercise was not advised because an increase in appetite usually follows increased physical activity[11]. Massage was not suggested since it has been proven to have no value in reducing weight nor measurements[12].

The basal metabolic rate decreased as weight loss increased. A maintenance diet did not bring this rate back to its previous level.

A nitrogen deficit usually occurs from the eighth to tenth week on the reducing diet. This balance is usually restored by the third or fourth week on a maintenance diet.

Overeating as a result of overbuying of food has become common, not only among the obese but even among those of normal weight. This is due to the increase and the rise of supermarkets and shopping centers. The former neighborhood grocery store is fast fading away. One now shops with a cart, which seems to be getting smaller and smaller for the larger amount of foods that are placed upon them. One refrigerator in the home is not sufficient any more. We must have a refrigerator and a freezer. The idea of shopping for a whole week is a good one but to consume the whole week's purchase in one or two days is not so good. The housewife today buys more food than she needs and to justify herself, more food is consumed by the family than they need. This has now become a contributing factor in a large measure to obesity and overweight.

Conclusions

1. Group therapy in weight reduction is satisfactory from the psychosomatic approach.

2. The length of time of the course was insufficient for persons who had 25 or more pounds to lose.

3. Follow-up methods must be devised to accomplish maintenance of the weight which was lost.

4. The number of patients breaking the diet was negligible compared to patients who do this in private practice.

5. The treatment of every obese individual must be oriented psychosomatically either by the family physician, internist or psychiatrist.

6. A great measure of success depends on the personality of the group leaders. This has been demonstrated by following the results of some leaders whose classes always show good weight losses as against other leaders who consistently show a poor response.

7. The supermarkets have become warehouses of groceries and meat products for each family to draw on. They are the contributing storage depots for future body fat.

Obesity has been an individual problem to each member. They have tried to lose weight many times by devious methods and fad diets without permanent success. Nearly all regained their weight within two years.

An important observation was that as long as these patients were part of a group they were losing weight without too much effort. But as soon as they were separated and had to go it alone, many of them regained their weight before a year was up. It becomes obvious then, that we should continue treating the obese by group therapy but develop a new approach or new technics which will have a more permanent effect.

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Discussion

Dr. Theodore S. Heineken (Bloomfield, N. J.):—I want to ask Dr. Kalb a few questions.

Why does smoking many times check the appetite in individuals? I have had a number of patients who say they increase their weight when they stop smoking.

Another thing, too, is that there is a simple exercise for reducing weight which you did not mention, and that is, halfway through a meal, I advise my patients to push themselves away from the table.

What per cent of success have you had in the group therapy as opposed to the private practice, where the patients pays for reducing?

Dr. Kalb:—As to the question of smoking, this does not inhibit the appetite. As you probably know, some of the fattest patients you have are very heavy smokers. The only thing is, when they stop smoking, it is easy for them to put on weight. For want of something better to do, they will raid the refrigerator or eat more sweets. They seem to eat more fattening food, but heavy smoking does not make much difference.

As to the per cent of failures, in the classes we had about 2 per cent, but in private practice it runs around 20 per cent.

REGIONAL ENTERITIS*

SAMUEL S. BERGER, M.D., F.A.C.P., F.A.C.G.†

Cleveland, Ohio

The purpose of giving the following case history is to mirror the background and the events leading up to the development of regional enteritis as we have known this disease. For the sake of brevity, I shall record only some of the essential features.

The patient, a 62-year old female has been under my observation for more than 30 years. Her general physical make-up is of the asthenic type, as were both her parents. She is emotionally labile and reacts poorly to stress, is a sensitive-type individual, easily depressed, readily upset by mental strain and psychic trauma.

Her outstanding complaints have been frequent nasal congestion with rhinorrhea, attacks of bronchitis, hives and migraine headaches, digestive disturbances, i.e., gaseous distention, bowel unrest, and frequent attacks of cramps and diarrhea.

In 1923, because of persistent indigestion, gas, belching and intestinal unrest, x-rays of the gastrointestinal tract were made. The esophagus, stomach and duodenum were negative. There was marked visceroptosis, emptying was rapid, the colon was negative. Gastric analysis—Maximum free 40, total 75. Occult blood was negative. Hemoglobin 78 per cent, R.B.C. 4,200,000. Urine was negative. Sigmoidoscopic examination revealed a normal-appearing bowel. Stool examinations were negative. This irritable gastrointestinal tract was thought to be on a functional basis and food allergy. Sensitization tests revealed the patient to be allergic to dust, moulds, dairy products and a number of other foods.

On August 2, 1925 patient complained of gaseous eructations, abdominal discomfort, at times cramps, no diarrhea. X-ray of the gastrointestinal tract was essentially negative. Sigmoidoscopic examination and barium enema were negative.

On September 20, 1930 there was a large amount of gas with rumbling and unrest in the bowels, diarrhea of two weeks' duration. Gastrointestinal tract x-ray series was negative. Impression—Functional gastrointestinal disturbances, probably gastrointestinal allergy.

Because of the persistence of abdominal pains, belching, marked tenderness over the abdomen and the presence of considerable apprehension, gastroin-

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†Consultant, Mt. Sinai Hospital.

testinal x-ray series was repeated on May 8, 1931 and found to be negative. Sigmoidoscopic examination was negative. Sensitivity tests were repeated and the patient was found to be sensitive to dust and moulds.

February 11, 1933, patient had an uneasy feeling in the intestinal tract, with rumbling and distention and diarrhea. Belching a great deal. X-ray of the entire gastrointestinal tract, including the gallbladder, and barium enema were negative.

On May 27, 1936 there was a complaint of cramps, pains that come and go intermittently. There was marked tenderness in the right lower quadrant of the abdomen. No elevation of temperature. Rectal examination revealed tenderness in both lower quadrants of the abdomen.

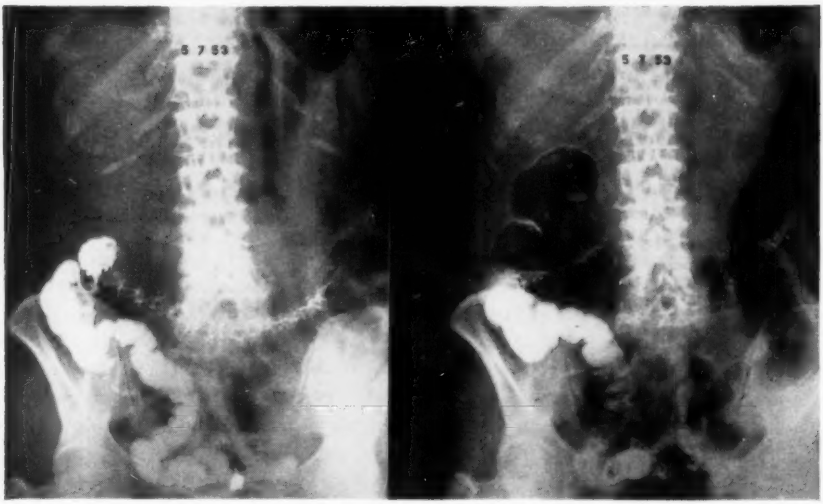

Fig. 1a

Fig. 1b

On May 26, 1937 the B.M.R. was 17 per cent. Patient was being desensitized for hay fever and house dust. Had an attack of asthma, coughing and has nasal congestion and frontal headaches. Turbinates and sinuses were congested.

Menopausal symptoms began September 21, 1938 with frequent headaches, cervical arthritis.

April 18, 1939, patient was apprehensive, with marked anxiety present. She continued to take shots for hay fever and dust. There were arthritic pains in the shoulder, cervical spine and right elbow. Abdominal discomfort continued and at times she had loose bowels and continued gaseous distention. Hgb.—81

per cent. 13 gm.; R.B.C.—4,710,000. B.M.R.—19 per cent. She was given small doses of thyroxine 1/320 gr. which she could not tolerate, as it produced anginal pains. E.K.G.—Normal record. Heart and lungs negative. B.P.—110/70. Urine negative.

On February 12, 1940 the abdominal discomfort was more intense and persistent. Gastrointestinal series were repeated and found to be essentially negative. Gastric Analysis:—Free acid 25, Total 35. Occult blood negative. Gained considerable weight.

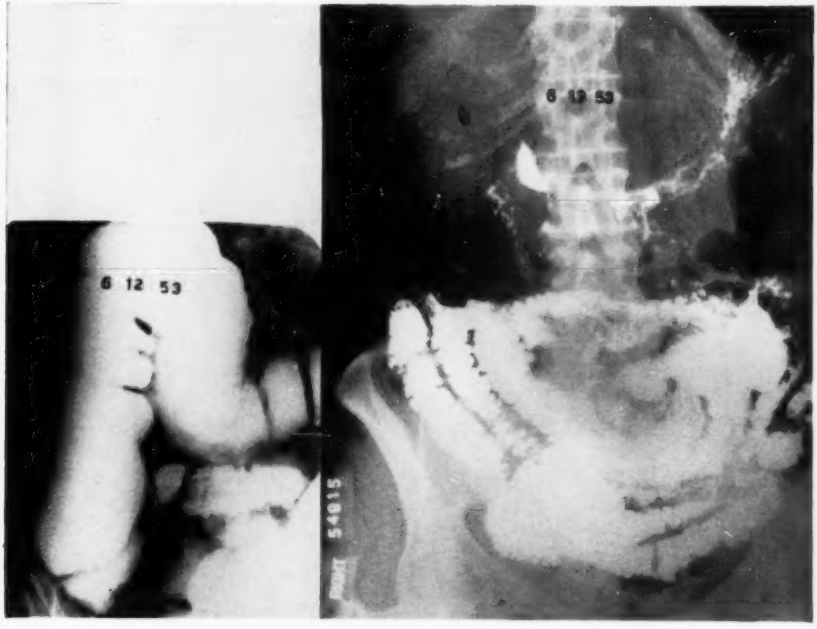

Fig. 2a Fig. 2b

On January 30, 1942 patient had severe headaches and her sinuses were congested. Intestinal unrest, cramps and diarrhea which patient attributed to seafood to which she is allergic were present. B.P. 130/80.

She complained of precordial pain and palpitation in June, 1943 and her B.P. was 130/90.

In August and September, 1944, she had rather severe hay fever.

Vaginal hysterectomy was done on February 19, 1945 with uneventful recovery. Feels depressed and jittery. General physical examination negative. Hgb.—80, R.B.C.—4,000,000.

June 26, 1945, she suffered anginal attacks which were relieved by nitroglycerine. E.K.G. was negative, B.P. 150/100.

March 24, 1947 there were loose bowels, cramps. Bowel unrest was quite troublesome. During this period, she had a good deal of nasal and sinus congestion. Turbinates were swollen and edematous.

In May, 1948 the B.M.R. was 11 per cent. There were bouts of hypertension, very labile blood pressure, ranging between 160-210/90. Tests for pheochromocytoma were negative. Physical examination—Heart, basal systolic murmur, lungs negative; moderate tenderness over the entire abdomen, B.P. 190/100,

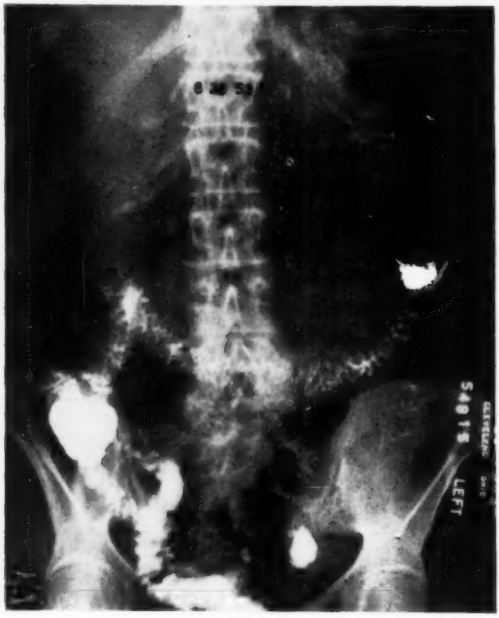

Fig. 3

polypoid turbinates. Sigmoidoscopic was negative. Esophagus, stomach and duodenum were negative. Colon was negative. Gallbladder normal filling and emptying. Gastric analysis—Free acid 35, total 61. Aorta slightly widened. Sl. l.v.h.

Sensitization tests were repeated. Patient was found to be sensitive to dairy products, figs, chocolate and many vegetables. Patient thought that Benadryl was quite helpful.

In March, 1949 her B.P. was 190/110. Ten minutes later, B.P. was 160, then 140/90. B.M.R. was 11 per cent. Urine showed a trace of albumen; N.P.N. 32.

The B.M.R. on January 28, 1950 was 12 per cent. During a virus infection, the patient developed a blood pressure of 220/130. Blood chemistry within normal range. Eye grounds negative. Allergic manifestations persisted. Considerable discomfort in the upper gastrointestinal tract. Blood showed a moderate hypochromic anemia. Arthritis in the cervical and lumbar spine. Sciatica.

Glycosuria was found in July, 1951. Sugar tolerance. Blood sugar fasting 103; ½ hour, 182; one hour, 190; two hours, 161; three hours, 90. Urine negative in all specimens. Gastrointestinal symptoms continued from time to time.

On January 30, 1951 the diarrhea became more and more persistent, some cramps. Gastrointestinal series repeated. Esophagus, stomach and duodenum

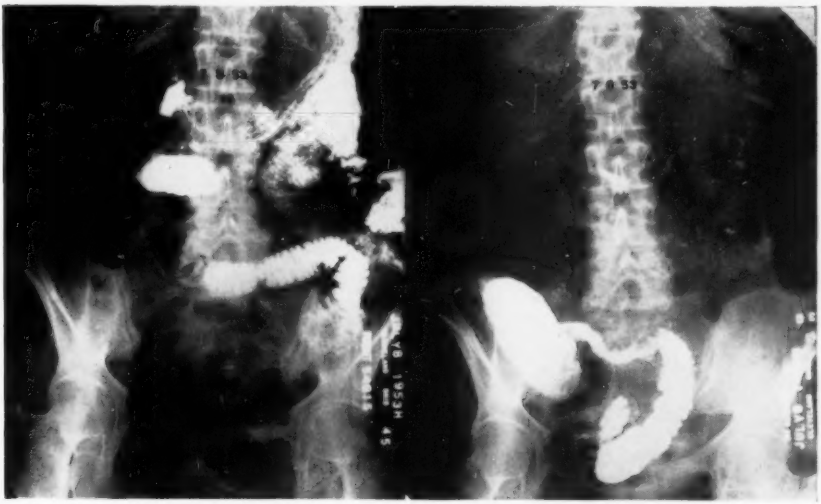

Fig. 4a Fig. 4b

were negative. The small intestine studies were negative. Sigmoidoscopic examination was negative. The gallbladder was negative. Considerable hypertrophic osteoarthritis of the spine was seen. B.P. ranged between 180 and 150 systolic over 100 diastolic.

Gaseous distention and bowel unrest were more or less constant, attacks of cramps and diarrhea occurred at frequent intervals. When the symptoms became more persistent and troublesome, studies of the gastrointestinal tract were repeated, 8 times between 1923 and 1953, since one cannot be sure that at the end of a year or two, the same condition must necessarily exist and also for fear of overlooking additional pathology.

The findings were essentially as on previous examinations; irritability and rapid emptying. The irritability of the small intestine is an expression of

constitutional and psychogenic factors which make it particularly susceptible to the introduction of an offending allergen. When this occurs, unrest, cramps and diarrhea result, which are due to edema of the bowel wall and may last for hours or days, depending on the severity of the reaction. It is completely reversible leaving no trace of its occurrence. These episodes recur again and again.

April 28, 1953, because of the persistence of the diarrhea and cramps and some slight loss of weight and strength, it was felt that there must be some pathology which, up to this point, we had not as yet discovered. A resurvey of the gastrointestinal tract revealed irritability of the entire gastrointestinal tract

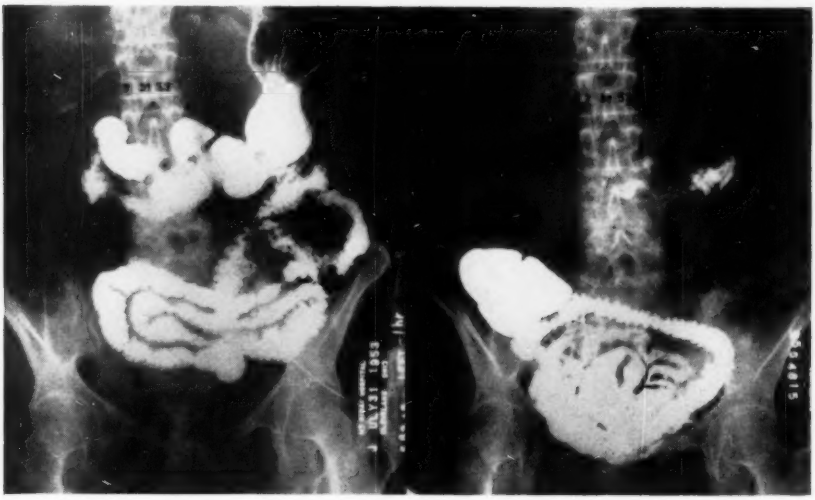

Fig. 5a Fig. 5b

with rapid transport of the barium column. Sigmoidoscopic examination and barium enema were negative.

On May 7, 1953 the diarrhea and cramps became more and more intense. The gastrointestinal tract was restudied and found to be, as heretofore, essentially negative. Barium enema and the terminal ileum by retrograde filling were negative. Stool examinations were negative. Gastric analysis—Free 39, total 83.

The cramps and diarrhea became so troublesome that hospitalization was suggested. Fever and chills developed. Cramps and diarrhea persisted and became increasingly more and more intense, the number of bowel movements reaching 18 to 20 in the 24 hours. The patient was admitted to Mt. Sinai Hospital, June 3, 1953.

At this time, she appeared acutely ill, dehydrated and toxic. Temperature was 104. She complained of a sense of weakness, considerable abdominal discomfort and distention. The bowel unrest and diarrhea were the chief complaints. Positive findings on physical examination were:—B.P.—164/98. Nasal mucosa boggy and edematous. Tacchycardia, pulse rate 110, a soft basal systolic murmur was present. The abdomen was somewhat distended, but only slightly tender. No masses were palpable. Pelvic examination was negative. Rectal and sigmoidoscopic examinations were negative. Barium enema and retrograde filling of the terminal ileum were negative. Considerable arthritic changes were

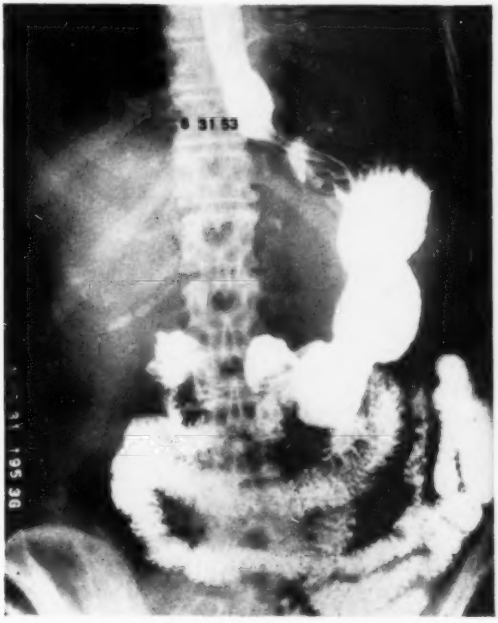

Fig. 6

noted in the lumbar spine. Agglutination tests were negative. Stool examinations were negative for parasites and ova. Cultures showed an overwhelming number of *proteus vulgaris*. There was a moderate hypochromic anemia, a leucocytosis reaching 16,500, an eosinophelia of 16 per cent.

The acute infection, the cramps and diarrhea persisted. X-ray studies were repeated. Findings—Fluoroscopic and film studies of the esophagus, stomach and duodenum were essentially negative.

There appeared to be some coarsening of the mucosal pattern of the small intestine, the exact etiology of which was uncertain. The terminal ileum was

not too well seen on the small intestinal study, but was adequately seen on barium enema examination and did not appear unusual. The coarsening of the mucosal pattern of the small intestine was thought to be due to a deficiency state, due to long-standing dietary restrictions. Clinically, suspected ileitis.

Because of the history of long-standing recurrent diarrhea which now became so intense, the presence of allergy, and the presence of a severe infection, it became more than a suspicion that an acute ileitis was present.

All indicated laboratory studies were made from time to time. These included: Complete blood, blood cultures: sedimentation rate which was increased to 60 mm. at the end of one hour was present in the beginning of the infection. A leucocytosis of 16,250 with 16 per cent eosinophiles was

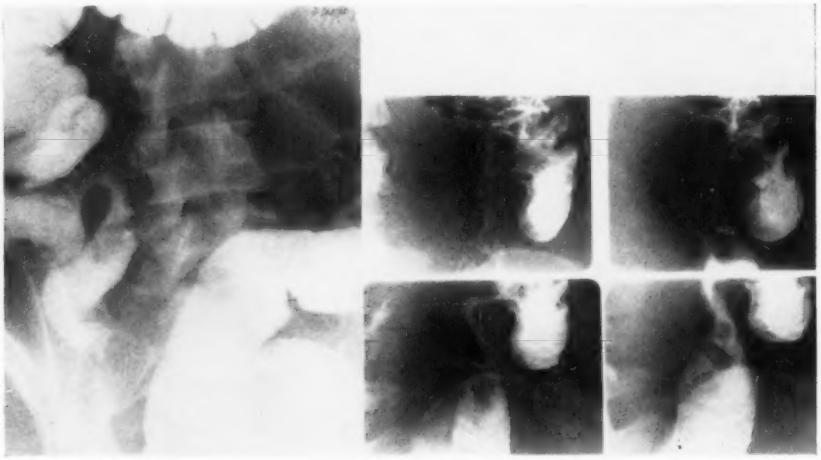

Fig. 7a Fig. 7b

present. Stool examinations, (warm specimens and direct smears from the bowel were negative for amebae or cysts) cultures revealed *proteus vulgaris* as the dominant organism in the fecal stream before antibiotics were used, and these organisms were found to be sensitive to neomycin, less so to streptomycin.

Electrolyte studies were made at very frequent intervals and a hypopotassemia with characteristic E.K.G. findings was present for a brief period. It was corrected by the administration of potassium chloride. Blood proteins dropped to albumen 2.4, globulin 1.7 during the course of the disease.

Although repeated stool examinations were negative for amebae, it was thought advisable to give the patient a course of antiamebic therapy, since she had but recently returned from Jamaica. The presence of 16 per cent eosino-

phelia count added to the suspicion of a possible parasitic infestation. A six-day course of milibis-aralen threapy failed to influence the course of the disease.

On July 8, about five weeks after admission, a third x-ray examination, particularly of the small bowel was made. The appearance of the upper small bowel at this time compared with its appearance previously showed the mucosal pattern to be better visualized, a reversal of the process in the upper small bowel. There was marked irritability as on the previous examinations. The slight changes in the small bowel pattern, coupled with the long-standing history of repeated attacks of cramps and diarrhea, the history of allergy, and the presence of a severe infection with no other definite findings seemed sufficient to make a tentative diagnosis of regional enteritis, not forgetting to consider lymphosarcoma and Hodgkins' disease. X-ray of the chest was negative.

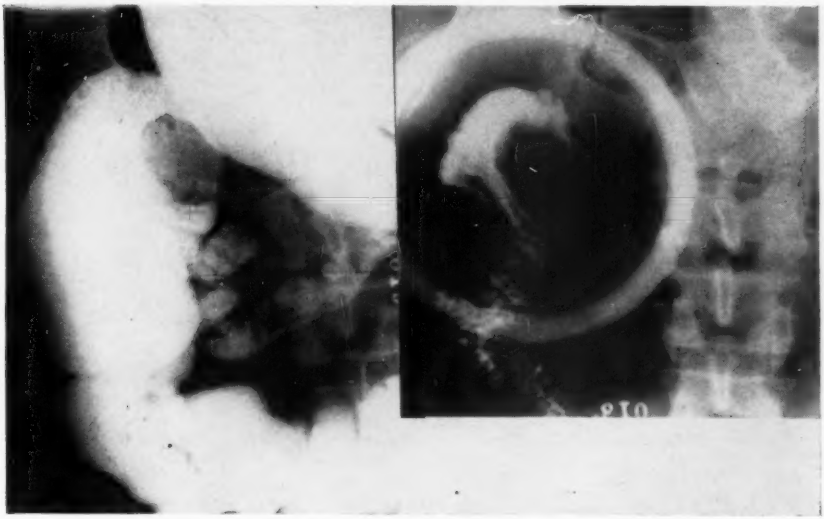

Fig. 8a Fig. 8b

Treatment was begun accordingly using general measures to improve the nutritional state, a high protein, high calorie, low residue diet, eliminating, insofar as possible, the offending allergens, maintaining the electrolyte and fluid balance in which there were changes throughout the course of this disease. Transfusions of fresh blood were given. Short courses of streptomycin and neomycin were given since the dominating organisms in the stool, found by direct smear and cultures were found to be consistently *proteus vulgaris*, sensitive to neomycin, less so to streptomycin. Although these antibiotics were used only for short periods of time, there occurred an overgrowth of yeast which invaded the pharynx. At present, we have broad spectrum antibiotics

which inhibit monilial overgrowth in the intestinal tract. Sulfathaladine in 8 gm. doses in the 24 hours was used without appreciable effect. Since Furadentin was successfully used in *proteus* infections of the urinary tract, we tried it in 150 mg. doses four times daily. After two days, however, it induced nausea and vomiting and it was discontinued. To aid in the treatment of the infection of the fecal stream, azulfadine was tried in 1 gm. doses every 3 hours around the clock. Since antibiotics were used simultaneously, its effect was difficult to evalute. Theoretically, its use is sound, since it penetrates and is absorbed through the intestinal wall where it is bacteriostatic.

The acute fulminating process persisted. The use of ACTH was begun with 20 units twice a day. The effect was dramatic. The temperature dropped, the

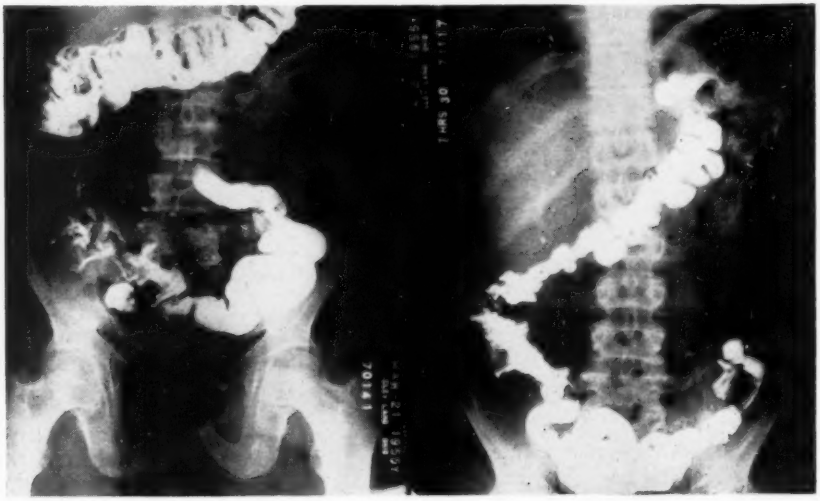

Fig. 9a Fig. 9b

diarrhea and abdominal symptoms diminished, a sense of well-being was experienced, appetite improved, all in all a remarkable change for the better. The dose of 20 units twice daily promptly proved to be excessive since the patient became hyperkinetic. The dose was gradually reduced to 10 units twice daily. Improvement was maintained and the dosage was gradually reduced until only 5 units a day, intermittently, was necessary to maintain this improved condition, when the natural recuperative forces took over. Cortisone was substituted for brief periods to prevent exhaustion of the adrenals.

Complications:—Erythema nodosum developed on both legs. The nodes were quite tender. *Erythema nodosum* is frequently seen with apical pulmonary tuberculosis. I believe more frequently with streptococcus infection. I have seen this association several times. X-ray of the chest was negative.

Acute arthritis of the wrists and ankles developed. Because of the high protein diet, gout was thought of as the possible etiology, but the blood uric acid was normal, 4.8 mg. per 100 c.c.

On July 30, 1953, eight weeks after admission to the hospital, x-ray of the small intestine revealed a more normal-appearing upper part. The transit time was adequate and there was continuity of the barium column, without any significant breaking up that one sees in vitamin deficiency states. In the lower ileum, however, for a distance of perhaps a foot and a half, and extending to the cecum, one notices a slightly irregular contour of the ileum. The folds here are definitely thickened and suggest a hyperplastic change. This region is fairly irritable and contracts markedly when manipulated. Pressure

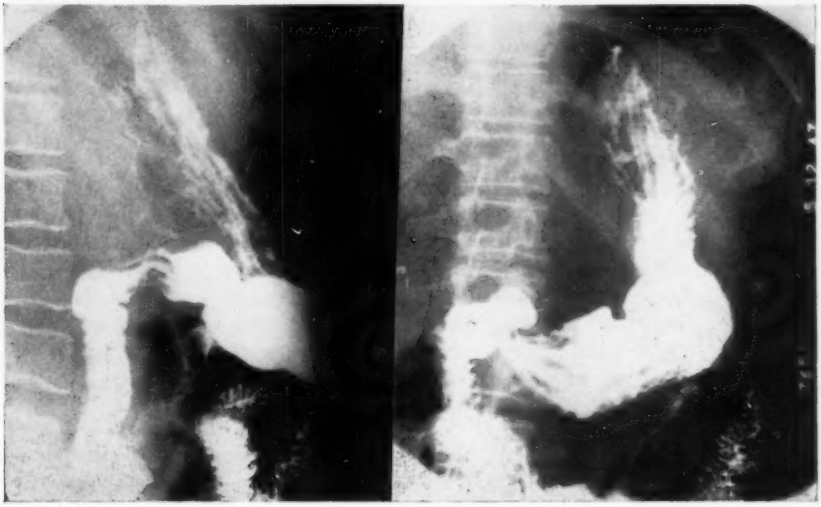

Fig. 10a Fig. 10b

studies over the area show the thickened course of folds quite well. The findings are certainly consistent at this point with hyperplastic regional ulcerative ileitis. Thus the fourth x-ray examination made 8 weeks after the beginning of an acute fulminating infection confirmed the presumptive diagnosis of ileitis made clinically earlier.

The patient's general physical condition was much improved and on August 1, 1953, two months after admission to the hospital, she was discharged. The diagnosis was definitely regional enteritis.

Her temperature remained normal, there was practically no abdominal discomfort present, only 2 or 3 semiformed bowel movements in the 24 hours. Stool cultures showed practically normal flora.

For a period of approximately one month, the patient remained improved, apparently progressing toward recovery, when she suddenly developed bleeding from the bowel which became massive, passing large amounts of blood and going into shock. She was readmitted to the hospital.

The blood count was 1.8. Previous count was 4.8. The blood pressure dropped to 70 mm. systolic. She continued to bleed, but by continuous transfusions, shock was sufficiently overcome to undertake an exploratory.

About 70 cm. of the ileum and 30 cm. of the cecum and colon were removed. The bowel appeared injected and filled with blood. Opening the specimen, the very characteristic cobblestone appearance of the terminal ileum was seen, with numerous superficial erosions on the mucosa. There was an abrupt line of demarcation of the diseased area above which the bowel appeared normal. The ileum was anastomosed to the side of the transverse colon.

Pathological Report

About 75 cm. of the ileum was removed and about 30 cm. of the colon. The pathology was limited to the terminal 30 cm. of the ileum and cecum. In this terminal portion of the ileum, the mucosa is markedly hyperemic and numerous small superficial erosions and some more penetrating ulcers are seen, the largest of which measured about .5 cm. in diameter. None of the ulcers appeared to penetrate to the muscularis. The mucosa of the cecum was also hyperemic and several scattered small ulcers were noted. As in the ileum, these ulcers were shallow and showed no evidence of penetration into the muscularis. The wall did not appear thicker and examination of the serosal surface showed no evidence of pathology.

Multiple sections revealed regional enteritis involving the terminal ileum and cecum, and portions of the transverse colon. There was edema and congestion in addition to the marked chronic inflammatory reaction. There was thickening of the wall with varying degrees of fibrosis in all the layers.

Postoperatively, particular attention was paid to the fluid and electrolyte balance. The blood count was brought up to practically normal with additional transfusions. The blood proteins were 3.8 albumen and 2.5 globulin. Sodium, potassium and chlorides were brought up to within normal limits. The bowel movements were 2 to 5 in 24 hours. Stool cultures still revealed an abundant growth of *proteus*. The patient made an uneventful recovery and was discharged in fair general condition, 14 days after surgery.

Two months later, the patient was readmitted to the hospital, because of the development of a firm, indurated mass in the abdominal wall, which was opened, and the wire sutures with the inflammatory surrounding tissue removed. Cultures from the wound revealed an abundant growth of Proteus.

In February, 1954, the patient developed a fecal fistula. Cultures from the tract and cultures from a catheterized specimen of urine also revealed *proteus vulgaris*. Because of high fever, tenderness and induration around the wound, the wound was again explored and a large amount of purulent material was expressed from the peritoneal cavity. A fecal fistula was found to go into the end of the transverse colon. The distal 8 inches of the ileum was infiltrated and the mesentery was thickened. The rest of the small bowel was free from disease. After resection, the ileum was anastomosed side-to-side to the transverse colon.

Examination of the gross specimen showed the mucosal surface of the terminal 17 cm. of the ileum to be thickened, hypertrophic, of a firm texture, almost granulomatous in nature. The wall at this area measured .7 cm. in thickness, while the remainder of the small bowel measured only .4 cm. in thickness.

A large multilocular abscess was found in the peritoneum March 7, 1954, containing thick, creamy pus. Smear revealed numerous small gram bacilli. Culture of the pus revealed a moderate amount of *E. coli*. Stool cultures showed an abundant growth of *proteus*.

A fecal fistula which had developed was finally closed on November 8 when an exploratory operation was done. A small fistula leading into the blind end of the colon was found. Examination of the small intestine revealed no recurrence of ileitis. The colon appeared normal. A rectovaginal fistula, which had been present, seemed closed. No thickening of the mesentery was found and the area of anastomosis was soft and patent.

After a stormy course, the patient was discharged December 1, 1954 in good condition.

She progressed favorably but still had bowel unrest with 3, 4 or more semiformed bowel movements daily. A good deal of gas was disturbing. Gain in weight and strength was slow, since a good part of the absorbing surface of the small intestine was lost. Readjustment to the altered bowel function was difficult and trying.

Due regard was paid to her diet, the offending allergens were eliminated insofar as possible. The continued mental and physical rest was helpful in promoting a return to a better state of health. In the course of several months, her general physical and emotional state was much improved.

Anticholinergic and antispasmodic drugs were used as indicated.

Comments

Regional or terminal ileitis is thought to be an inflammatory and cicatrizing disease, usually of the terminal ileum or other areas of the small bowel,

and occasionally extending into the large bowel. Several areas may be involved simultaneously with normal or so-called skip areas intervening. This is the pathology we have come to recognize when the disease is relatively advanced. The earliest stage of this disease is not an inflammatory process but is an edema of the mucosa of the intestinal wall, an allergic phenomenon inducing bowel unrest, cramps, gaseous distention and loose bowels which may last for a matter of hours or days, leaving no discernible changes in the affected bowel which returns functionally to normal. The process is completely reversible and is followed by periods of freedom only to recur again and again. The intervening periods of freedom may last weeks or months. In these early stages, x-ray examinations of the gastrointestinal tract will reveal irritability with rapid transport of the barium column, otherwise essentially negative. These early changes are not seen pathologically since they do not come to autopsy, nor is surgery necessary in this stage.

These periods of remissions and reactivations occurred many many times in the 30-year period of observation of this patient, and during a 15-year period of observation of another typical patient who developed insidiously a progressive narrowing and stiffening of the bowel wall of the terminal ileum, as seen on x-ray. These are irreversible changes due to a low-grade chronic infection, producing fibrous tissue proliferation and cicatrization, progressing to partial obstruction.

When the inflammatory process has progressed, the cramps and diarrhea become more persistent, and the pathological changes have advanced, the slightly ragged contours of the ileum can be seen on x-ray, especially proximal to and extending to the cecum. The mucosal folds become definitely thickened and suggest a hyperplastic change. This region becomes quite irritable and contracts markedly when manipulated. Pressure studies over the area show the thickened folds quite well.

Still later, the irregularity of the involved terminal ileum becomes more pronounced, the rigidity and narrowing progresses until the terminal ileum is so narrowed that it has been described by Kantor as the "string sign". This, along with the obstructive phenomena which is then present is characteristic of terminal ileitis. It is an advanced stage and it is no longer reversible. The optimum time for medical management has been lost.

During the stage of acute infection, ulcerations, abscess and fistula formations are frequent complications. Ulcerations may lead to bleeding which may be slight, and usually passes unnoticed, leading eventually to a hypochromic anemia. Rarely, the bleeding may be massive, inducing severe shock and threatening life. It must then be treated promptly and energetically with adequate replacement of blood, and resection, if bleeding continues and if urgency demands it.

Pathological changes are slow and insidious, based on several possible factors, particularly allergy and infection. Early uncomplicated attacks are merely edema of the intestinal wall due to intestinal allergy. It is completely reversible, leaving no trace. A survey of 600 cases by Bargen and associates showed allergy to be a frequent finding. While this frequent association does not prove that ileitis is due to allergy, it does suggest a probable relationship; the local tissue sensitivity forming a favorable soil and in conjunction with other factors, particularly infection, play an important role in the production of the disease characterized by fibrosis, narrowing and partial obstruction. The early stages of this disease go unrecognized. Infection of the fecal stream induces lymphatic hyperplasia and blockage, decreasing resistance of the mucosa which may lead to ulceration. The pathological process extends from the serosa into the mesentery and lymph nodes and progresses into abscess and fistula tract formation. The disease is usually limited to the ileum. Occasionally, however, the large bowel becomes involved.

Reichert and Mathes experimentally produced lesions simulating regional enteritis by lymphatic blockage. This process was intensified by intravenous injection of bacteria. The lesions were most evident along the mesenteric border of the bowel which is the point of exit of the lymphatics. If infection of the fecal stream is an important factor, it is to be expected that the greatest damage to the bowel wall should occur at the point of the greatest concentration and activity which is just above the ileocecal valve. Through greatly accentuated activity of the bowel in this region, local trauma aids infection and inflammatory reaction. The ileocecal valve in most instances acts as a barrier to the disease process and hinders its extension into the cecum.

Histological Features

All the layers of the bowel may eventually become involved, the mucosa, the submucosa, the serosa, as well as the mesentery and lymph nodes. At first, there is edema, then cellular infiltration and dilatation of the blood and lymph vessels which is most marked in the submucosa, where characteristic tubercles were described by Warren and Summers. This process is still reversible, but when the disease progresses, and chronic infection is added to the lymph edema, inducing hyperplastic fibrous tissue formation, ulceration, obstruction, abscess and fistula formation follow.

Diagnosis

We have as yet no means of recognizing regional enteritis in its early stages, when it is reversible. A history of recurrent attacks of abdominal pain, gaseous distention and diarrhea in an allergic individual particularly, should arouse suspicion of its presence. Repeated gastrointestinal x-ray series during the course of months and years may be necessary before irreversible changes de-

velop and become manifest in the ileum on x-ray examination. When acute infection is added to the picture, the pathologic changes may progress rapidly, inducing changes in the mucosal pattern of the small bowel.

There is progression from edema to inflammation, ulceration, thickening and stiffening of the bowel wall with irritability over the involved area. It took about 8 weeks for these changes to become marked enough to become recognizable on x-ray after the acute, virulent infection had set in.

All the clinical symptoms become aggravated, fever at times reaching 105°. Chilly sensations or chills may be added. The intestinal symptoms become markedly aggravated. Abdominal unrest and pain, distention and as many as 18 to 20 bowel movements in the 24 hours may occur in this acute phase.

The clinical symptoms and the x-ray appearance in this acute phase are compatible with lymphosarcoma and Hodgkins' disease of the small bowel. A long-standing history of recurrent attacks of abdominal pain and diarrhea, however, especially in an allergic individual, and an eosinophilia when present, are important differential diagnostic features.

Figure 8 shows numerous small patches of lymphoid hyperplasia which appears granular and a rather large intramural mass in the cecum. They were removed and the pathological report was lymphosarcoma.

Figure 9a shows lymphosarcoma of the terminal ileum and cecum. Operative removal and pathological report.

In Figure 10 the area of constriction of the duodenum extends to the ligament of Treitz. Operative removal and pathological diagnosis, Hodgkins' disease. Hodgkins' disease of the small bowel may be widespread suggesting an inflammatory disease, or it may be localized like carcinoma. The dominating symptoms may be cramps, diarrhea and fever.

Granuloma of the small bowel is a relatively rare disease. The terminal ileum is the most common site of involvement but other portions of the ileum may also be involved along with the mesentery and lymph nodes. Roentgenologically, in the advanced stage, there are dilatations of loops of small bowel retaining opaque material for some hours (Stout and Marcuse). Lymphosarcoma tends to infiltrate the outer coats before involving the mucosa, causing no stenosis. The reverse is true of regional ileitis; there, the disease progresses from edema to fibrosis and stenosis.

In the pre-Crohn era, I recall several cases presenting abdominal pain, right lower quadrant rigidity, with or without diarrhea, fever and palpable mass, where the diagnosis was appendicitis, only to find at operation, a granuloma of the terminal ileum and cecum, of undetermined etiology. In retrospect, these were instances of advanced terminal ileitis.

I recall one case particularly seen in 1916, of a patient with high fever, abdominal pain, tenderness and distention, and bloody diarrhea, in whom a diagnosis of typhoid fever was made. The Widal, however, remained negative. Then a tentative diagnosis of tuberculosis of the cecum was made. Months later, an exploratory operation revealed a granulomatous mass involving the terminal ileum and cecum of undetermined etiology. Abscess and fistulous tract formations necessitated in the following years, several surgical procedures. Finally, the correct diagnosis of terminal ileitis was made. After 39 years, this man is still alive, but unfortunately, considerably incapacitated.

Treatment

Treatment will depend upon the stage in which the disease is recognized. The diagnosis of ileitis in the early stage is practically never made, so the treatment is merely symptomatic. Measures to improve the general health, appropriate diet, eliminating the offending allergens insofar as possible, the use of antihistamines, antispasmodics and anticholinergics, and now tranquilizing drugs, is helpful.

If seen in a later stage, when the condition has been recognized but is still reversible, the judicious use of hormones and now the newer corticosteroids in addition to the above measures is exceedingly helpful.

When acute infection is added to the picture, the use of appropriate broad spectrum antibiotics, depending upon the sensitivity of the predominant organism in the fecal stream, must be used. The nonabsorbable sulfas in adequate amounts can still be used with benefit. Azulfidine is preferred in the acute stage.

In acutely ill patients with high fever, marked toxemia, severe abdominal cramps, 18 to 20 bowel movements in 24 hours, ACTH produced a most dramatic response. All the symptoms were suppressed practically immediately and a sense of well-being was established. We have learned that relatively small dosage is adequate: two ten unit doses in the 24 hours may be sufficient. This can be decreased as rapidly as the symptoms will permit. As little as 5 units in 24 hours may be adequate in maintaining this improvement in conjunction with other aids, supportive measures, antibiotics and transfusions, until the natural recuperative forces take over and a remission occurs. Since ACTH and cortisone are not curative, they must be used merely as aids in turning the tide toward recovery.

The complications which have been attributed to their use were due, I believe, mainly to overdosage, prolonged and injudicious use. These complications have occurred even before these hormones were known. The question of the use of ACTH has been debated for fear of masking symptoms, preoperatively, and postoperatively and delaying healing. We should not lose, in these stress situations, particularly, its beneficial effects and the support it lends in

tiding the patient over these critical periods. In short, I believe that ACTH and the newer corticosteroids are a most valuable adjunct to our armamentarium.

To control the cramps and the diarrhea, cautious use of small doses of tincture of opium and belladonna are the most effective.

It is very important to maintain the fluid and electrolyte balance and the blood protein levels during the acute phase of the disease. Repeated transfusions are of intestimable value.

The emotional state of the patient is important. Tranquilizing agents may be helpful. We must strive to attain a good psychological adjustment to the altered physiology resulting from the loss of considerable portion of the small intestine, ileocecal valve and part of the colon after surgery has been necessary.

Summary

So-called regional enteritis in the early uncomplicated stage, is merely an edema of the bowel wall, completely reversible and subject to recurrences over a period of years. It occurs most frequently in the younger age group, but no age is exempt.

In its etiology, allergy appears to be the most important single factor. A long-standing history of recurrent attacks of cramps and diarrhea in an allergic and emotionally unstable individual should arouse suspicion that it may be a manifestation of an early stage of regional enteritis.

The irritability of the small intestine is a manifestation of constitutional and psychogenic instability. Thus the small intestine becomes highly susceptible to cholinergic trigger-mechanisms, histamine, bacterial or psychogenic disturbances.

When infection of the fecal stream occurs, then inflammatory changes occur, usually at the point of the greatest concentration and activity which is just above the ileocecal valve. Repeated attacks will eventually lead to irreversible changes and complications.

The inflammatory reaction may be low-grade and chronic, or acute, virulent and fulminating. In the case of the 62-year old woman detailed, a virulent infection occurred after 30 years of recurrent attacks of cramps and diarrhea. The dominating organism in the fecal stream was found to be *proteus vulgaris*. Further bacteriological studies of the fecal stream are necessary to determine the relationship of this, or any other organism in the production of this disease.

After the onset of acute infection in the case detailed, it required four x-ray series in the course of 8 weeks to reveal recognizable changes, particularly in the terminal portion of the ileum. It is well to bear in mind, if the disease

is suspected, that several series of x-ray studies may be necessary before a definite diagnosis is possible.

The chronic case, typified by a highly allergic 30-year old woman, with numerous recurrences during a 15-year period of observation, of frequent attacks of abdominal pain and diarrhea, progressed insidiously, and when last seen, the x-ray of the small bowel revealed a narrowing of the terminal ileum, the stenosis producing partial obstruction, a combination which we have come to recognize as typical of terminal ileitis. It is no longer reversible and becomes a surgical problem. Ways and means must be sought to make the diagnosis earlier. Repeated x-ray studies, especially of the small bowel, are necessary to demonstrate the complete reversibility of this condition in the early phases, as well as to make it possible to detect irreversible changes when they occur.

X-ray studies of the small bowel, before, during, and after attacks of cramps and diarrhea should reveal irritability with rapid emptying, coarsening and thickening of the mucosal folds due to edema during the attack and complete reversibility after the attack. Tallant, O'Neill, Urbach and Price have demonstrated these changes by including in the barium meal the offending allergen.

In every stage of the disease, bacteriologic studies of the fecal stream are necessary to detect changes in the intestinal flora, so that appropriate measures can be instituted.

The early treatment of the infection and the elimination of the offending allergens may prevent the later irreversible changes and its complications.

ERRORS IN ANORECTAL PROCTOLOGY*

JOHN F. KEANE, M.D., F.I.C.S., F.A.C.G.

Boston, Mass.

Anorectal Proctology encompasses within its sphere a juxtapositional harmony of diverse[17,22] anatomical structures[6] and physiological activities. Accordingly it is affected directly or indirectly by any normal activation or abnormal change in function and structure of most of the body. It is the recipient of normal and disturbed metabolism and bacterial and chemical pathology, not only of the entire gastrointestinal tract, but also of the respiratory system. It is not uncommonly the revealer of pathology elsewhere[10,27,30]. It controls, by the electronics within its scope, the important physiologies of defecation and continence. The electronics contained here also demonstrate their communion with electronics of other locations in the gastrointestinal tract, i.e. in the gastrocolic reflex. Meleney quotes Whipple as stating that not until anorectal pathology was eliminated did ileostomy assume the role for which it was originally intended. Appreciating these facts, the concept of error in anorectal proctology predicates a large potential, a few salient features of which I shall attempt, within my allotted time, to mention. Let us briefly review the factual generalities of a few symptoms and clinical findings classically associated with anorectal pathology.

Tumors:—Blumer's Shelf[4], endometriosis, metastases from thyroid and chest lesions, adnexal pathologies, amebiasis, the colitides, tuberculosis, lues and lymphogranuloma venereum. *Atony* of the sphincter and incontinence from cerebrospinal or cord lesions; senility and severe anemias.

Pruritus:—Leukemia, diabetes, extrahepatic obstructive jaundice, gallbladder pathology, allergy, purpura, hormone imbalance, sex maladjustment, stress, avitaminosis, pancreatitis, sympathetic nerve irritation, changes in bacterial flora, Addison's disease, senility, antibiotic therapy[31].

Bleeding:—Ulceration of any portion of the gastrointestinal tract[27,30], abdominal trauma, thrombocytopenia, Osler-Rendu disease or telangiectatic phenomena, hepatogenous jaundice, polio, renal crises—as lower nephron nephrosis, aneurysm, avitaminosis and hormone imbalance.

Pain:—May be the initial symptom of infectious hepatitis; seen in intestinal obstruction; cord and osseous lesions, stress syndrome (*proctalgia fugax*), endometriosis, ureteral crises, metastasis and sciatic nerve involvement.

Odor:—Magnified in, or may be the only symptom, initially, of schizophrenia.

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History

A careful history is an integral part of valuable information from which a correct diagnosis is based. To avoid errors, pertinent information should include: 1. *Familial:*—Blood dyscrasias; polyposis, congenital defects[1,2], infections, malignancies, psychoses, and, if delayed convalescence—the reason. 2. *Past personal:*—Travels; gastrointestinal episodes; trauma, previous examinations, diagnosis, consultations and therapy results. Experience with antibiotics and chemotherapy, anesthesia, quinine, parenteral medication, transfusions, blood dyscrasias—as jaundice and bleeding tendencies, allergies, body reaction to emotion, alcoholism, changes in weight, bowel habit, strength, appetite and sleep. Special examinations as sigmoidoscopy, radiology, laboratory, including serology and results. The patient may forget. You should not. 3. *Present personal:*—Error is displayed here if—1. Chief complaints are not fully evaluated. 2. Symptoms presented formulate one's mind into deciding upon a bigoted physical examination. 3. A snap diagnosis is concluded solely upon symptoms, especially so if expressed to patient. 4. There is a failure to correlate past and familial history to present complaints[27]. 5. The relationship of symptoms presented with phenomena of the genitourinary or reproductive systems; or alteration in metabolism and blood are ignored. For example, dysuria in nerve pathology, pain in endometriosis, bleeding in thrombocytopenia, pruritus in leukemia, or exaggerated hemorrhoidal symptoms in liver inefficiency. 6. There is failure to recognize symptomatology as local manifestations of a general pathological[9] entity possibility.

Clinical Examination

General:—Indifference as to:—1. General appearance, color as in jaundice, pigmentation of lips[28,29] (possible polyposis or telangiectasis) weight loss, elevated temperature, pallor, puffy facies or obesity, diverticulosis, diabetes, liver and cardiovascular possibilities, Cushing's syndrome, tourniquet test during blood pressure estimation. 2. Abdominal examination as a routine procedure frequently by-passed. To detect distention, masses, tenderness, dehydration, spasms, etc. 3. Inguinal gland evaluation is rarely considered. The few moments taken in these steps may definitely determine entirely, or in gradation, coupled with local examination—a. Consultation or referral possibility[9]. b. Type of radiology or laboratory procedure. c. Aid in prognosis. d. Therapy—if medical, suitable steps including collaboration in therapy with confreres. If surgical—whether to be delayed or abandoned, except in an emergency. If elective—whether ambulatory as injection; or hospitalization as operative. e. Possibility of overlooking infection (pulse and temperature very important here). f. A definite step in diagnosis.

Local Examination

Lethargy here is an error[2,11,12,15,18]. *Inspection:*—A meticulous inspection of the area should be made for wasting, dehydration, specific skin abnormalities[2], a search for concealed openings and ulcerations, evaluation as to infection,

trauma, incomplete or fistulous sinuses, prolapsing pathology, bleeding and discharge and their character; and scars, their complications and extent.

Palpation—external[12,15]:—For concealed tumors (buttocks, ischiorectal, etc.) abscesses (as sphincteric) and fibrosis; their character, extent and complication. *Digital examination*[2,16]:—An important step—as frequently the revealed pathology may be found by no other means. This examination is in error: 1. If it is performed in a stabbing manner, disregarding sphincter tone. 2. Unless it searches in a rotating, widely sweeping arc, and includes every part of the musculature; ano canal; rectal lumen and wall, and adjacent structures with thorough evaluation. 3. Unless it reaches as far proximal as possible. 4. Unless it is performed in the jackknife position. 5. Unless it includes a bimanual examination. Digital examination is unique in its ability to discover the existence and characteristics of certain tumor entities, intramural and extramural[16], and the degree of mobility and density of pathology. Moreover prognosis and therapy are often largely determined by its deductions. Consequently indolence in its completeness is a grave error.

Sigmoidoscopic examination[2,11,27]:—Neglect of this is an error. Its invincible aid in diagnosis demands it to be: 1. Obligatory in every examination, and, if indicated, supervised properly during the entire manipulation. 2. Performed by or supervised by one possessing, a. Knowledge of the area. b. Experience in the mechanics of examination. c. The ability to appraise properly what is viewed[7]. d. Skill and judgment in indicated therapy, and intelligent acumen concerning indications for radiology and the laboratory procedures to be ordered. 3. Conducted in an ideal environment, and after proper preparation. 4. A repeat maneuver if no examination for eight months; previous report negative or doubtful; and regardless of whether the pathology has been previously treated or untreated. 5. Performed prior to surgery unless the previous examination was complete and recent. If a noncooperative patient, or if the examination is to be followed by immediate surgery, hospitalization is essential. A necessary adjunct is smear or biopsy by snare or punch[2,11]. It is necessary also to differentiate whether it is dysfunction or definite pathology, and to enable correct evaluation as to location, extension, and characteristics and complications[14]. Proper hemostasis after biopsy must be considered through this means. Air insufflation is rarely necessary. It is contraindicated in the elderly; in severe ulceration; diverticulitis; or other causes of wall thinness. A history of shock experience after enemas; weakness, faintness, etc., should automatically bar its use. The maneuver is fraught with danger as to perforation; intraabdominal crises, and circulatory embarrassment. Forceful passage in the debilitated; the colitides; narrowed lumen; very nervous or uncooperative patient; wall immobility; or in haste, courts disaster.

Barium Enema

This procedure has a definite position in diagnostic progress[2]. It should be intercalated in all clinical examinations. To deny this is an error in anorectal proctology.

Indications:—1. Any pathology or atypism noted in anorectal and sigmoidoscopic examinations. 2. Suggestive abdominal or local symptoms even if sigmoidoscopic examination is negative.

Laboratory Studies

Failure to do complete laboratory studies is an error. This may include uropepsin, electrolyte, serial, microscopic, urobilinogen, indices, cultures, pathogen antibiotic sensitivity titer, blood group, and Rh factor. Feces examination including color, occult blood, parasites, fat, pH and predominant organism. These may be regarded not only as necessary, but a competent diagnosis is incomplete unless the results are studied. We frequently encounter the fact that the final diagnosis may be the unique containment alone of the pathologist.

As experience accumulates during the years, enhanced by day after day contact with pathology and dysfunction, arrayed against numerous complaints, factual or hypothetical, cynicism gathers momentum, discuss this as we may. One of the nonexcusable errors in anorectal proctology is to allow this cynicism to divert or becalm proper judgment and efforts by the label "psychotic". Reflection warrants proof that abortive or hasty and ignored continuity in correct diagnostic procedure produces the triad of: 1. Fallacious decisions. 2. Inefficient therapy. 3. Questionable results.

Injection Therapy

To avoid error do not encourage this as a permanent therapy because: 1. It presents a vista of an indefinite repeated therapy. 2. Courses of treatment usually at one or two-year intervals may be disappointing to the apprehensive patient, and the initial course economically may equal total for a surgical procedure. 3. Pathology, as crypts, fibrosis, etc., retained. This encourages continued infection which too often aids in hemorrhoid pathology[18]. 4. Allergy reactions are always a possibility. 5. Tumor production—as carcinoids, has been claimed. 6. Ulcerative slough with bleeding, pain, tenesmus, with renewal of cancer phobia in the patient, has been observed. 7. Prolapse of injected area on coughing, straining, lifting, especially if mucosa redundant, is a possibility. 8. Postinjection impaction has been described. 9. Stricture formation especially if infection proximal or general, (colitides or lymphopathia) has received comment. Indications for it are if limitations are explained and if patient thoroughly understands these, and definite reasons exist. a. *Palliative:*—Surgical hazards as senility; severe cardiac or psychoses; or individual problems of health. b. Hospitalization is absolutely refused. c. Family responsibilities exist. d. Temporary improvement in general condition occurs, awaiting selective surgery. e. Economic. f. Postoperative retention of hemorrhoids—This, provided pathology is minor.

Precautions:—1. Never inject without an extraordinary reason until a complete examination as outlined has been satisfactorily completed, and an intelli-

gent diagnosis has been procured. 2. Injective therapy requires on the part of the operator—surgical knowledge, experience, skill, judgment, care, and contraindication mindedness. In fairness I will concede one possible advantage to this therapy, namely, it offers a positive step in check-up observation.

Errors in Surgery

Errors in operative procedure through sigmoidoscopy[14] include: 1. Positive therapy despite improper preparation. 2. *Polyps:*—Snaring all of pedicle. If sessile, attempting the entity. This procedure should be left to a skilled and experienced operator. Better to take biopsies, wait for report, and if benign use electrotherapy. If malignant one must seek consultation. 3. Being overzealous in the use of electrotherapy. Fulguration with the bipolar current courts bowel wall necrosis, and eventual perforation if excessive. Several treatments are preferred with appraisal before each treatment. 4. Dessication or dehydration, monopolar may be slower but is safer. It is not as penetrating. 5. Being heedless of explosive gas and flash potential. Suction before and during electrotherapy is strongly encouraged. Recent papers should be reviewed concerning the use of CO_2 gas[3,17]. 6. Disregarding proper evaluation and reflection before therapy on the question whether tumors benign in character, 20 to 25 cm. proximal to the anal verge, should be treated through the sigmoidoscope from below. This is a controversial point. Sigmoidotomy (colpotomy) by abdominal approach, with the advantage, if so considered, of viewing pathology through the sigmoidoscope inserted in the incised bowel, which may be missed in radiology examination, and the proper appraisal of any accompanying existent pathology, is a superior technic, preferred surgical judgment, and in my mind is conducive to pleasant dreams.

In general errors in surgery are caused by [19,24]: 1. *Vague diagnosis:*—a. Total dependence on the diagnosis of a confrère. b. Indifference to history and reports. c. Superficial clinical examination. d. Lack of indicated consultation. 2. *Routine preoperative preparation*[20]*:*—It must be individualized. 3. *Indifference to proper environment:*—a. Hospitalization and asepsis. b. Proper illumination and instruments. c. Capable assistance and anesthesia. d. Adequate emergency[29], laboratory and radiology facilities. 4. Surgery *per se* is considered as a minor procedure, hence it is delegated to someone possessing incomplete knowledge of anatomy, specialized and varied technics[13], surgical requirements and the pitfalls of this important area. Add to these lack of supervision and the results are usually as expected, with repeat surgery mandatory. 5. *Premature Surgery:*—a. Indifference as to wisdom of any surgery at the time. b. Impatience with conservative regime. c. Disregard for, or ignorance of, practical pathology[18]. d. Ruled by patient's wishes. 6. Lack of skill, asepsis, or timing in the local injection of aqueous or oil soluble anesthetics. 7. *Errors in suture technic:*—Tying too tightly. Too much tissue inclusion in one suture. If ties break this is a warning of excessive pressure

exerted. Too many sutures. Large needles and bulky sutures. The more sutures the more bleeding. If not immediately postoperative, it will be encountered as tearing during or after the first defecation, when infection will also be apparent, and a possible return trip to surgery is demanded. 8. *Improper hemostasis:*—This is overcome not by tissue crushing, sutures and ties, but by patience, pressure, and attention to bleeding points. 9. *Excessive anal dilatation:*—It promotes anatomical or fibrotic tissue dissolution, resulting in hemorrhage, infection, delayed healing, excessive fibrosis and stenosis, and potential incompetence. 10. Undue haste. 11. Excessive tissue removal[8]. This often produces unnecessary pain, delayed healing and convalescence, and deep scar formation; gas incontinence and wet anus are possibilities as are stenosis and resistant pruritus. Therapy of any kind should only be instituted after proper and complete examination, as previously outlined in this discourse.

Errors in Hemorrhoidal Surgery

These include: 1. Routine use of clamp and cautery. 2. Rough handling in tearing of tissues. 3. Carelessness in muscle preservation[6]. 4. Crown sutures placed too high, in the same plane, too deep or with too broad a "bite". Do not include part of the adjacent hemorrhoid nor the muscle in this suture. Step-toe these, each one slightly above or below the other. Carelessness in the snug tying of these sutures. 5. Failure to crush the hemorrhoidal pedicle before excision. 6. Hemostasis neglected after the excision of each hemorrhoid. 7. Removing the so-called three classical hemorrhoids, and allowing others to remain. This is incomplete surgery. 8. Oversight in nonremoval of concomitant pathology[2,18,25] as papillae, crypts, fibrosis, tabs, etc. Office operative procedures postoperatively are inconclusive, and may be embarrassing. 9. Failure to perform posterior sphinctotomy[26] when indicated. *Advantages:*—Drainage; pain and spasm reduced; it aids defecation and early ambulation; there is minimized evidence of fibrosis and postoperative fissure. 10. Inadequate drainage[8]. 11. Suturing excised areas, although practiced by many competent proctologists, would seem to the essayist to promote hematoma, infection, localized phlebitis, inadequate drainage and increased morbidity. 12. Excessive packing, with prolonged retention of bleeding is bothersome. In personal experience the Buie pack is offered as a distinct advantage. Remove it in 24 hours.

Postoperative Errors

1. Failure in prompt and efficient pain relief. 2. Retarding of early ambulation, early postoperative defecation measures, digital appraisal. 3. Ignoring daily inspection and speedy convalescence requirements. Indifference as to prompt attention to surgical records. Complete when memory is fresh. This induces satisfactory future reference.

Summary

Anorectal proctology concerns proper diagnosis, therapy, and restoration of normal function in a vital area, comprised anatomically and physiologically of widely diverse structures and functions activating or activated by many generalized body relationships and stimuli. The concept of errors in anorectal proctology contains a large potential. They usually stem from a human equation triad: 1. Indolence in history and complete examination. 2. Egotistical fantasy with a woeful display of inadequate knowledge, unskilled technic and nonsupervision, the offspring usually of a biased judgment. 3. Indifference or ignorance in the all important postoperative care.

Sequence:—1. History lapses. 2. Clinical indifference and even neglect of essential sigmoidoscopy, radiology, laboratory procedures and consultations. 3. This incompetence presents natural failure of proper appraisal; obviously produces records and diagnoses of little value, thus leading to faulty and ineffective therapy, and convalescence or postoperative care and check-ups, embarrassing, abortive, and even forgotten. The concensus of opinion, judging from the varied results of therapy in this field, and the expressions of those who have experienced this therapy, indicates three grave errors:—1. The incomplete complicated results attained especially in proctologic surgery, due to the gross misconception that anorectal procedures are of minor import. This encourages a paucity of knowledge and indifferent implementation or supervision adopted in therapy and restoration of function, with its obvious corollary of unnecessary complications and undesirable sequellae. 2. Much of the original pathology remains[18], plus new pathology added, implying mandatory repeat surgery. 3. The reaction of the patient; exaggerated recounting of unnecessary experiences and inappropriate therapy with economic loss, and the knowledge that further surgery is required for what was primarily believed to be *minor* surgery. The danger lies in the fear this engenders in the laity, not only as to anorectal surgery, but even to examination. This may very well nullify percentage-wise efforts in malignant education.

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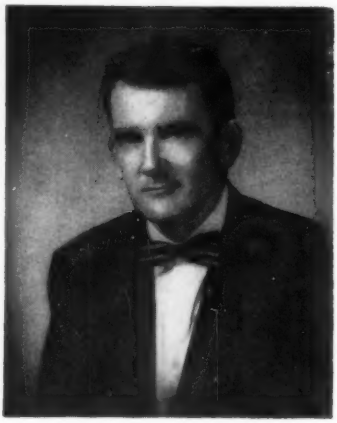


President's Message

The programs for our 1956 Convention and Course have been completed and you will be pleased at the excellent job Dr. Frank J. Borrelli has done. Members of our Ladies Auxiliary have been planning an exceptional social program extending from the 15th through the 20th of October in New York City.

At the recent April meeting of the Board of Trustees of the American College of Gastroenterology it was voted to establish chapters of the College with the requirement that each member of the chapter be a member in good standing of the American College of Gastroenterology. The Committee on activation of chapters consists of Dr. Joseph Shaiken, chairman, Dr. Irving A. Levin, Dr. Joseph Roger Van Dyne, Dr. S. Bernard Kaplan and Dr. F. H. Voss, and is to prepare recommendations for the establishment of chapters and the granting of charters, and to report back to the Board of Trustees at their next meeting. This move was made to provide year-round activity and to facilitate regional meetings.

The Trustees also discussed measures to give our members and associate fellows a greater voice in the management of the affairs of the College. In particular this has reference to allowing members to advance to associate fellowship by attending and satisfactorily completing a specified number of postgraduate courses, approved by our Committee on Postgraduate Education.

Your Trustees and Governors solicit your opinion on these matters and welcome any suggestions you might have.

I. T. Nif

ABSTRACTS FOR GASTROENTEROLOGISTS

GASTROINTESTINAL TRACT

ORAL LESIONS CAUSED BY ANTIENZYME DENTIFRICES: William B. Simms. U. S. Armed Forces M. J. 6:995 (July), 1955.

Recently various antienzymes have been added to commercial dentifrices. Individual sensitivity to the antienzymes occur with the production of many bizarre-like changes.

Primary symptoms consist of an irritated, painful mouth associated with a tingling or very sensitive tongue.

Examination usually reveals a tender, raw, beefy red tongue and an oral mucosa varying in appearance from moderate redness to severe leukoplakia.

Differential diagnosis consists of herpetic stomatitis, *herpes simplex* and occasionally carcinoma. Frequently there is denudation of the buccal mucosa and a pale or whitish film is exfoliated. In appearance this white plaque somewhat resembles lichen planus and a slight leukoplakia. Involvement of the soft palate usually consists of papillary, vesicular lesions that appear to be tiny mucus cysts.

The most important factor in diagnosis is a history of the use of antienzyme dentifrices.

It is postulated that the antienzymes, in addition to neutralizing the enzymes necessary to bacterial growth, also neutralize some of those enzymes which are beneficial to the existence of normal oral epithelium.

Summaries of three cases are reported to illustrate the typical history, symptoms and characteristics of the syndrome.

Joseph E. Walther

DIAGNOSTIC PNEUMOPERITONEUM: S. C. Truelove and K. Lumsden. Brit. M. J. 4939:585 (3 Sept.), 1955.

The authors point out that diagnostic pneumoperitoneum is not used as frequently as it might be and that it is of considerable value. They discuss the method of induction in patients with and without ascites and describe their own particular technic. In their discussion of radiologic technics, they point out that prone as well as supine studies are needed.

They discuss the radiographic appearances in alcoholic cirrhosis, biliary cirrhosis, peritoneal metastases of neoplasm, retro-

peritoneal tumors displacing the spleen, and pleural effusion mimicking high left diaphragm. In their discussion, they indicate the obvious contraindications, such as congestive heart failure with no respiratory reserve.

IRVIN DEUTSCH

ESOPHAGUS

CURRENT ADVANCES IN DIAGNOSIS AND TREATMENT OF ESOPHAGEAL HIATAL HERNIA AND ACHALASIA OF THE ESOPHAGUS: Herman J. Moersch. J.M.A. Alabama 25:9 (July), 1955.

Moersch reviews the Mayo Clinic experience in the diagnosis and treatment in esophageal hiatal hernia and achalasia of the esophagus. Their experience would seem to indicate that hiatal hernia occurs in at least one and one-half per cent of the population in the United States. The ageing process and obesity are felt to be the most important contributing factors. In their experience, 25 per cent of all hiatal herniae are asymptomatic and in another 25 per cent the relationship between the hernia and symptoms was difficult to establish; in the remaining 50 per cent, the hernia gave rise to definite clinical symptoms. The three common types are discussed, namely, the short esophagus with intra-thoracic stomach, the paraesophageal hernia and the sliding type. The latter makes up 67 per cent of all cases. Sixty-five per cent of patients will be relieved by a conservative medical program. In achalasia, Moersch has found that approximately 70 per cent of patients will be completely relieved of their difficulty by the use of Plummer Hydrostatic Dilator; 20 per cent will be improved but will require repeated dilatations and approximately 10 per cent are not helped by this method of treatment. When a surgical approach is necessary, the Heller procedure, in which the circular muscles of the cardia are cut, has proven most satisfactory.

JOHN M. MCMAHON

CLINICAL AND RADIOLOGICAL CORRELATIONS WITH OPTICAL ESOPHAGOSCOPY: Stephen J. Stempien, Angelo Dagradi, Donald M. Sanders and Rudolf Schindler. J.A.M.A. 159:22 (Sept. 3), 1955.

This study reports the experiences of the authors in 172 cases esophagoscoped with the Schindler instrument using a rubber-tipped flexible obturator. Comparative studies of cases in which both x-ray and esophagoscopy were done indicated a superiority of endoscopy over roentgenology with respect to esophagitis, hemorrhagic erosions, gastritis within hernial pouches, telangiectasia, in certain cases of esophageal varices and hiatus hernia and in the facility for taking biopsies. The x-ray examination was found to be superior in the diagnosis of esophageal diverticula and in certain instances of esophageal varices and hiatus hernia.

The authors stress the fact that where symptoms indicate esophageal disease, both x-ray and esophagoscopy should be performed—that the two modalities are complementary and in no sense competitive. Esophagoscopy with the flexible rubber-tipped obturator resulted in only one minor complication in 197 endoscopies.

WM. K. BILLINGSLEY, JR.

STOMACH

EXSANGUINATING HEMORRHAGE FROM PEPTIC ULCER: Burns Plewes and Allan D. Pollock. Canad. M. A. J. 13:73 (1 July), 1955.

The authors review a series of 62 cases of hemorrhage from peptic ulcer from the Toronto General Hospital. Of these, 44 responded to conservative measures, and were not operated on and 18 had to be operated on to control blood loss. The authors then summarize all 18 cases that were operated on. All were done as emergencies. None were refused operation because of age or poor condition. Of these all but three survived, one died from pulmonary embolus and two from massive

hemorrhage. If massive gastric hemorrhage continues the earlier the operation the better the chance for success.

In discussion of these cases operated on the following conclusions were reached: Persistent and massive hemorrhage is more likely in the older and artereosclerotic people. The younger person may stop bleeding by himself. Warnings of trouble to come were common in most of these histories, such as exacerbation of ulcer symptoms, pain, indigestion, etc. Wound complications are very common in this series of patients.

LOUIS K. MORGANSTEIN

EXPERIENCE WITH SUBTOTAL GASTRECTOMY IN PEPTIC ULCER DISEASE. H. L. Bockus, J. L. A. Roth and W. S. Haubrich. Rev. Brasil Gastroenterol. pp. 723-732, 1955.

The authors' experiences have been satisfactory when using the Billroth II high subtotal gastrectomy. Their analysis suggests even better results where the resections are of three-fourths or more of the stomach. Present day operative mortality was found not to exceed 2.5 per cent and the recurrence rate was equally low (2.3 per cent). Undesirable postgastrectomy sequellae was the principle reason for continuing to seek a more satisfactory operation; and this was found as a sequel in no more than 5 per cent of the patients. The authors think that this latter figure could be reduced even more by the judicious selection of patients.

J. R. VAN DYNE

THE SIGNIFICANCE OF HORMONAL FACTORS IN THE PATHOGENESIS OF PEPTIC ULCER: S. J. Gray. Rev. Brasil Gastroenterol. pp. 771-780, 1955.

Although the gastric response to stress is undoubtedly mediated through the vagus nerve, the evidence presented by the author suggests that an additional hormonal mechanism is involved which is intimately associated with the General Adaptation Syndrome.

Chronic emotional and physical stress will stimulate the stomach to secrete increased acid and pepsin by way of a humoral mechanism involving the hypothalamic pituitary-adrenal-gastric axis independent of the vagus nerve or the gastric antrum. There appear to be significant hormonal influences in addition to neural stimuli in the pathogenesis of peptic ulcer. Potentiation of the hormonal pathways may explain the mechanism by which ulcers may recur in patients whose vagus nerves have been satisfactorily severed. Other factors mentioned by the author in the pathogenesis of ulcer are: gastric motility, tissue resistance and vascular factors as yet not determined.

J. R. VAN DYNE

CIRCULATORY AND NERVOUS FACTORS IN THE ETIOLOGY OF ULCER: R. S. Boles. Rev. Brasil Gastroenterol. 795-800, 1955.

The authors make no claim that the sole cause of ulcer may be abnormalities of the circulatory system whether these be functional or organic, or due to the altered chemical composition of the blood. However, one can no longer ignore the fact that these disturbances do proceed and even bring about alterations in the motor and secretory mechanism of the digestive tract that favor ulcer production. The author suggests that the term "peptic ulcer" be abandoned and that the adherence to the theory of "no acid—no ulcer" be relinquished.

J. R. VAN DYNE

ETIOPATHOLOGICAL DIFFERENCES BETWEEN GASTRIC, DUODENAL AND JEJUNAL ULCERS: H. Shay. Rev. Brasil Gastroenterol. pp. 801-806, 1955.

The author points out that gastric and duodenal ulcer influence gastric motor and secretory functions quite differently. Yet this difference is not due to fundamental differences between gastric and duodenal ulcer, but rather to the effect of the ulcerative processes upon physiological mechanisms that happen to be housed in the

mucosal areas involved.

Marginal ulcer occurring as it does on the jejunal side of the stoma, can develop only if a "satisfactory" gastric anacidity does not follow the subtotal gastric resection and represents the acid pepsin effect on a portion of the intestinal mucosa even less well equipped to resist such action than is the mucosa of the duodenal cap.

J. R. VAN DYNE

THE RESULTS OF MEDICAL TREATMENT OF PEPTIC ULCER: C. A. Flood. Rev. Brasil Gastroenter. pp. 1001-1008, 1955.

The author discusses his experience with the results of conservative management of peptic ulcer at The Presbyterian Hospital in New York. Medical therapy in uncomplicated ulcer is usually followed by a satisfactory immediate symptomatic response. Gastric ulcer usually heals in about seven weeks. The healing time of duodenal ulcer may be a little more rapid.

A slow symptomatic response to treatment is sometimes related to emotional problems or to severe anatomical damage. Often, however, there may be no explanation for intractability.

The long range results of medical treatment of ulcer are much less satisfactory than the immediate results. The average recurrence rate is approximately once every two years. An initial slow response to treatment is a bad prognostic omen and these patients are usually more prone to experience frequent recurrences. A history of multiple hemorrhages is a serious prognostic sign. After two or more hemorrhages, the risk of further bleeding is approximately doubled. Persistent pyloric obstruction in a small series of cases conservatively managed was attended by a generally unsatisfactory course. Carcinoma of the stomach developed in five out of 101 patients with benign gastric ulcer, who were followed on conservative medical therapy.

J. R. VAN DYNE

INTESTINES

DISCUSSION ON TOXIC AND NUTRITIONAL DISTURBANCES IN THE SMALL INTESTINE ASSOCIATED WITH SURGERY OF THE GASTROINTESTINAL TRACT: Harold C. Edwards. Proc. Roy. Soc. Med. 48:245 (Apr.), 1955.

Serious small intestinal sequelae may follow surgery anywhere but especially abdominal operations. A chart illustrating small intestinal disorders following surgery of the gastrointestinal tract is listed in the article.

The paper next treats of postoperative malabsorption states. These are dangerous potential complications in any gastrointestinal-surgical therapy. The chief offender is short-circuiting anastomoses, as well as where extensive small intestinal resection is practiced and the evaluation should rest upon the length of intestine *remaining* because the size of relaxed bowel after resection is misleading.

In the discussion, Prof. L. J. Witts stated that defective absorption of iron and Vitamin B_{12} inevitably follows loss of the stomach but that pernicious anemia is rare after partial gastrectomy or gastroenterostomy. However, macrocytic anemias have been known to be delayed from 2 to 17 years following surgery.

Corry feels that necrotizing enteritis following partial gastrectomy was an infection which could involve a considerable group in one ward and which he attributes to *staphylococcus aureaus*. Those which follow surgery within three or four days are the most virulent and give rise to the highest mortality rates.

REGINALD B. WEILER

THE APPARENT ACTIVATION OF SALMONELLA ENTERITIS BY OXYTETRACYCLINE: Donald Finger and W. Barry Wood, Jr. Am. J. Med. 18:839 (May), 1955.

A 53-year old white male received Terramycin and Tetracycline following surgical repair of a Dupuytren's contracture of his hand. Previous history was negative except for three mild episodes of diarrhea during the preceding year attributed to food pois-

oning. On the fourth postoperative day fever, chills, headache and malaise appeared together with pain, rigidity and tenderness of the right lower abdomen and watery diarrhea. Stool cultures showed a heavy growth of *Salmonella muenchen* highly resistant to the administered antibiotics. The prophylactic use of these substances was not only of no help but actually endangered the patient's health by increasing his susceptibility to the latent salmonella infection.

H. B. EISENSTADT

MANAGEMENT OF POSTOPERATIVE PSEUDOMEMBRANOUS ENTEROCOLITIS WITH SHOCK: Ole T. Jonassen, Sidney M. Fierst and John J. Cincotti. New England J. Med. 252:792 (12 May), 1955.

Clinically the symptoms suggested those seen in Asiatic cholera, especially the great dehydration which persisted in spite of attempted replacement. Based on this, ACTH and cortisone were given for 48 hours in spite of some danger of bacterial dissemination. Erythromycin and chloramphenicol were directed against the staphylococcic invasion.

The serum bilirubin, with evidence of hepatocellular damage, was elevated because of impairment of liver function due to shock. Degenerative renal tubular pathology gave rise to casts, red and white blood corpuscles and albuminuria in the urine. Acute hypertensive attacks were due to sudden mobilization of nor-epinephrin contained in extracellular fluids which was distributed through diuresis.

Blood pressure must be restored to normal limits for the patient when the shock state has caused decrease in it. Nor-epinephrin restores the systolic values if given in adequate amounts. Then fluid and electrolytic balances are brought into relationship. In the early stage, broad-spectrum antibiotics are discontinued. Later erythromycin is exhibited even before bacteriological studies are completed. Bacitracin may be also employed.

The second therapy phase is related to supportive principles. Whole blood transfusions and serum albumen are utilized to overcome the protein deficiency. Intravenous caloric values are best met with dextrose and levilose. ACTH is also useful in the repairative process, and may safely be given when decreasing temperature and falling stool–bacterial counts indicate that the infection has been controlled. Lactobacillus preparations help restoration of normal intestinal flora. Testosterone seems to aid in restoring a positive nitrogen metabolism.

REGINALD B. WEILER

THE ACUTE ABDOMEN: Philip Thorek. Conn. State M. J. 19:449 (June), 1955.

Seven conditions account for 90 to 95 per cent of the pathology which make up acute emergencies within the abdomen. They are: 1. Acute appendicitis; 2. Perforated peptic ulcer; 3. Acute cholecystitis; 4. Acute salpingitis; 5. Acute hemorrhagic pancreatitis; 6. Renal colics; 7. Acute coronary disease.

In discussing the diagnosis of acute appendicitis, the author stresses three things: 1. Diffuse epigastric distress which localizes to the right lower quadrant within 24 hours is acute appendicitis until proven otherwise. 2. Anorexia is the most common symptom associated with acute appendicitis. 3. Acute appendicitis does not produce right rectus rigidity.

Only an underlying mass can make one rectus feel rigid. He reminds the reader that in the presence of a perforated peptic ulcer, duodenal or gastric contents may leak downward along the so-called paracolic gutter of the ascending colon, pool around the appendix, precipitate pain and tenderness and the removal of a reddened but innocuous appendix, while the perforated ulcer continues to leak with ensuing disaster.

He restates the important diagnostic and therapeutic considerations involved in the other five causes of 90 to 95 per cent of abdominal emergencies.

MILTON M. LIEBERTHAL

CHANGING CONCEPTS IN THE TREATMENT OF DIVERTICULITIS: Stephen E. Reid and Clarence M. Workman. Quart. Bull. Northwest. Univ. Med. Sch. 29:190 (Summer), 1955.

The authors believe that a radical surgical approach to diverticulitis of the colon offers better results than the conservative surgical procedures accepted heretofore. Diverticulitis should be considered in any patient over 40 with left lower quadrant distress, possibly with fever and diarrhea. Diverticulitis may be associated with rectal bleeding, at times of massive character. Of cases with diverticulitis 77 (29 per cent) had blood in the stool, the bleeding being profuse in 12 patients. Sixty-two (23 per cent) had obstructive symptoms. In differentiating diverticulitis from carcinoma a barium enema is the most important aid but is helpful in only 50-60 per cent. In 25 per cent of cases it is impossible to differentiate the two conditions even with the lesion in hand.

Conservative surgical procedures fail in about a third of patients with complications of diverticulitis. Minimal procedures are performed as emergency measures and the patient returns to his former state of chronic discomfort. The authors believe that complete diversion of the fecal stream must be done to allow the inflammation of the sigmoid to subside. This can be accomplished by a transverse colostomy with complete transection of the colon. With complete diversion of the fecal stream, in diverticulitis no appreciable discharge is noted in the distal segment after one week, while in cancer the bloody discharge continues. The transverse colostomy should be followed by resection of the sigmoid although this may have to be postponed for many months. Primary resection of the sigmoid in uncomplicated diverticulitis is quite safe with the use of antibiotics, skilled anesthesia, expert water and electrolyte balance and proper preoperative preparation. However, resection during obstruction should rarely be performed because of the increased risk and poor condition of the patient and the bowel wall. Adequate early resection of the involved colon rids the patient of his disease and offers more favorable results in morbidity and mortality than the more conservative approach.

ARNOLD STANTON

LEIOMYOSARCOMA OF THE JEJUNUM, WITH TWO CASE REPORTS AND A REVIEW OF THE LITERATURE. Guy W. Horsley and R. L. Means. Ann. Surg. 141:799-806 (June), 1955.

Leiomyosarcoma of the small intestines is also one of the rarer diseases of the gastrointestinal tract. The authors undertook the laborious task of analytically cataloguing 108 known cases from the literature. The location was: duodenum 33 cases, jejunum—38, ileum—24, not specified—15. The pathologic differential diagnosis from other neoplasmata, especially fibrosarcoma, can only be made by using special, i.e. van Gieson, stain.

Leiomyosarcoma is a slowly growing tumor, situated submucosally and producing mucosal ulceration. The predominant clinical features are: intestinal bleeding, palpable mass, rupture with peritonitis, cutaneous sinus-formation, intraperitoneal bleeding, intestinal obstruction, intussusception and metastasis, especially to the liver and peritoneum, weakness and loss of weight.

The first case presented was a 69-year old male patient with a 1½ year old history of weakness, loss of weight, intermittent tarry stools and constipation and a palpable mass in the upper left quadrant, at times changing in size. On operation a large mass originating from the jejunum about 10 cm. from the ligament of Treitz was resected. The central part of the tumor contained a large cavity with necrotic hemorrhagic walls, the cavity communicated with the intestinal lumen. The second case was a 65-year old female, who previously was operated upon because of jaundice as a possible extrahepatic obstructive jaundice. No neoplasma or stones were found and a T Tube was implanted in the common duct. Nevertheless after a short interval her symptoms, especially pain, jaundice, vomiting and finally tarry stools reappeared. On re-operation a large mass of the jejunum three feet from the ligament of Treitz was removed and histologically diagnosed as leiomyosarcoma.

In a bleeding leiomyosarcoma of the small intestines it is rather difficult to find the location of a tumor in the early stages, even on detailed small bowel studies. Mucosal irregularities, later on a filling-defect

and fistulous communication of a tumor cavity with the bowel, may be seen.

If in a given case of obscure gastrointestinal bleeding a laparotomy is performed and the origin of the bleeding is not found in the usual places, a thorough exploration of the small bowels should be done to exclude early leiomyosarcoma.

HANS J. JOSEPH

PROPHYLAXIS OF BOWEL CANCER: Maus W. Stearns, Jr. Clin. Med. 2:599 (June), 1955.

It is possible to practice prophylaxis of cancer of the colon and rectum by detecting and eradicating a premalignant lesion, the polyp, by which is meant a true glandular neoplasm, an adenoma arising from the mucosa of the bowel. Their detection is primarily by means of sigmoidoscopy, minimum indications for which are: 1. Any bowel or anal symptoms; 2. Any complete "check-up" or cancer detection examination; 3. Familial history of gastrointestinal polyp or cancer; 4. All patients over 35. For the portion of the colon beyond the reach of the sigmoidoscope, double-contrast x-ray studies are indicated under the following conditions: 1. Bowel symptoms unexplained by sigmoidoscopic findings; 2. Incomplete examination, or the demonstration of a polyp or flecks of blood by sigmoidoscopy; 3. Unexplained anemia or persistent occult blood in stools; 4. Familial history of gastrointestinal cancer or polyps.

Eradication of these lesions is the province of the general surgeon and proctologist. Removal of all lesions discovered would reduce the incidence of bowel cancer by over 50 per cent, which would reduce the number of deaths from this form of neoplasm more than all of our currently acceptable methods of treatment of established cancer.

All patients who have had one or more polyps should undergo periodic examinations for the remainder of their lives.

ARNOLD L. BERGER

FOOD ALLERGIES: DIAGNOSIS AND TREATMENT: Lydia A. DeVilbiss. Clin. Med. 2:593 (June), 1955.

Of the types of allergies (inhalant, contact, thermal, and ingestion), those due to foods can result in the most serious manifestations and complications. The ability to produce allergic symptoms by ingestion of selected foods or exposure to certain products helps rule out other causes for the manifestations. Among the important diagnostic symptoms are edema of any portion of the body or the effects of edema. There is generally an eosinophilia. Among the tests for food allergies are the elimination ingestion test, the food diary, rotary diversified diets, elimination diet lists, skin tests, and W.B.C. tests, a simplified form of which is described. Ingestion of an allergic food on an empty stomach will cause a drop in the W.B.C. of about 1,000 cells within an hour. The next day, the initial decrease of an allergenic food will be followed by the allergic toxic reaction and an increase in the W.B.C. to two or more times the patient's normal. Insofar as treatment is concerned, the use of drugs is chiefly symptomatic. Of prime importance is the elimination of causative factors.

ARNOLD L. BERGER

GASTROINTESTINAL COMPLICATIONS OF ANTIBIOTIC THERAPY: Charles T. Stone, Sr. and Marcel Patterson. Texas J. Med. 51:305 (June), 1955.

The authors note the following effects on the gastrointestinal tract:

1. Toxic effect—due to overdosage or direct irritation on the mucous membrane of the gastrointestinal tract. This causes anorexia, nausea, vomiting, diarrhea. These are more frequent with broad spectrum antibiotics.

2. Sensitization or allergic manifestation.

3. Nutritional deficiency—interferes with synthesis of Vitamin B and K. This may be due to greater demands of vitamins by organisms in the gastrointestinal tract or impaired food intake from anorexia, nausea, vomiting, etc.

4. Reaction to contaminants—such as pyrogens and histamine-like substances, etc.

5. Interference with cellular enzyme sys-

tem of the body.

6. Superinfections—all forms of broad spectrum antibiotics reduce the number of B. coli in the intestines, permitting overgrowth of other organisms, normally present in small amounts and clinically unimportant.

Treatment is difficult. Polymixin B, sulfa, or neomycin orally may inhibit growth. The majority of patients recover spontaneously within a week or so when the causative antibiotic is stopped. Beneficial results will be obtained by a bland low residue diet, antispasmodics, sedatives, etc. Buttermilk may or may not be helpful.

The most serious complication is from infection from overgrowth of staphylococcus or micrococcus strain. Therapy consists of discontinuing the antibiotic being given and starting immediately with erythromycin, neomycin or bacitricin orally and employing measures for control of circulatory failure.

Candida albicans may or may not be due to use of broad spectrum antibiotics. The two most common clinical manifestations are Thrush and skin infections. When antibiotics appear to be the causative agents, good results may be obtained by use of the newer antifungal antibiotics, Mycostatin which shows promising results against *candida albicans*.

LOUIS K. MORGANSTEIN

GENERALIZED GASTROINTESTINAL POLYPOSIS: Leonard W. Cronkhite, Jr. and Wilma Jeanne Canada. New England J. Med. 252:1011 (16 June), 1955.

Gastrointestinal polyposis can be classified into two types: Familial (polypoid adenomatosis of the colon, and Peutz-Jeghers syndrome of intestinal polyposis with melanin spots of the oral mucosa, lips and digits), and Nonfamilial (single or multiple adenomatous polyps, and generalized gastrointestinal polyposis).

The authors report two cases which showed generalized gastrointestinal polyposis, pigmentation of the face, neck and hands, alopecia and onychotrophia (atrophy of the fingernails and toenails), together with abdominal pain, nausea, vomiting and diarrhea. The disease progresses until intestinal absorption is so reduced that nutrition is impossible and the patient starves to death. The authors believe that a generalized deficiency state develops due to the extensive polyposis of the gastrointestinal tract.

ARNOLD STANTON

CANCER OF THE COLON: Arthur W. Allen, Claude E. Welch and Gordon Donaldson. West. J. Surg. 355 (June), 1955.

Cancer of the colon now approaches cancer of the stomach as a cause of death. This increased incidence is probably related to the increased life expectancy, the average age of the patient being about seven years higher than it was 15 years ago. Early surgical treatment greatly improves the curability as the five-year survival rate; which is proportional to the time interval between onset of symptoms and hospitalization. Salvage rate is greater when the regional lymph nodes are not involved by tumor. Approximately 80 per cent of the patients with negative nodes might some day be curable. In these cases hemicolectomy does not improve the prognosis over local resection. Spread beyond the gut requires en block removal provided there are no distant metastases. Palliative procedures are also frequently useful as the average duration of life after surgery is about nine months. If the resection is done as far as feasible a "second look" recommended by Wangensteen is not advocated. Preoperative preparation must be careful. Sulfathaladine, eight grams, daily for five days is the only chemotherapeutic agent used. If the routine preoperative stool culture reveals staphylococci the most suitable antibiotics determined by sensitivity tests are added.

H. B. EISENSTADT

MESENTERIC THROMBOSIS: N. B. Jaffee. Med. Times 83:567 (June), 1955.

The symptoms are: acute, violent abdominal pain; early emesis; bowel dysfunction; ileus; followed by shock. Symptoms suggesting internal hemorrhage are rarely absent. With the intestinal obstruction and peritonitis leucocytosis occurs. The bowel is usually silent. It is not unusual to be able to palpate a tumor at the site of the circu-

latory obstruction.

A ruptured mesenteric artery is heralded by sudden cramps followed by nausea and vomiting which later becomes hemorrhagic, as does the concommitant diarrhea. The pain is resistant to morphine. Rebound tenderness is more pronounced than palpitory discomfort. Pain is out of proportion to physical findings but when shock is also an early finding diagnosis of this catastrophic disease should be considered.

Immediate surgery is usually urgent, should not be postponed, and should be followed by anticoagulants, antibiotics, transfusion, cortisone and utmost care. The lowest recorded mortality rate is listed at 66 per cent.

X-ray may suggest obstruction. Enemas which contain occult blood or frank blood is important for diagnosis.

Differential diagnosis includes exclusion of: spontaneous retroperitoneal hemorrhage, rupture of the deep epigastric artery, idiopathic infarction of the greater omentum and rupture of the abdominal aorta.

REGINALD B. WEILER

TECHNICS IN FORCED ENTERAL FEEDING: Richard B. Magee. Pennsylvania M. J. 58:579 (June), 1955.

There are numerous ways in which food and water may be introduced into the gastrointestinal tract in seriously debilitated medical and surgical patients. The author gives specific directions for the technic of nasogastric tube feeding by urethral catheter, Levin tube, Lahey tissue drain, and emphasizes polyethylene tubing as the method of choice for this type of feeding. Gastrostomy and jejunostomy feeding methods are detailed. Homogenized milk alone is emphasized as the best all-around nutrient for these various types of forced feeding. Several illustrative cases are given.

JACOB A. RIESE

LIVER AND BILIARY TRACT

RECENT PROGRESS IN BILIARY TRACT SURGERY: Frank Glenn: Texas J. Med. 51:247 (May), 1955.

In this article the author discusses the progress made in the last 25 years in biliary tract surgery in general and also his experiences at New York Hospital–Cornell Medical Center. This progress is attributed to several factors. 1. The better understanding of biliary tract pathology and symptomatology. 2. The possibility of being able to make an exact diagnosis. 3. The better preoperative preparation of the patient, especially corrections of electrolite disturbances, the preoperative insertion of a Levin tube, and the wise use of antibiotics. 4. The addition of Vitamin K to the surgical armamentarium. 5. The flexibility in surgical technics. 6. Stated indications for exploration of the common duct. 7. Modern anesthesia greatly contributes to operative safety. 8. Silent stones, especially those of the large variety, should be removed. 9. It is better to operate while the patient is still younger, nevertheless advanced age does not constitute a contraindication to even prophylactic biliary surgery any more.

HANS J. JOSEPH

INFECTIOUS HEPATITIS: Gordon W. Grace. Texas J. Med. 51:244 (May), 1955.

After having shortly familiarized the reader with the history of infectious hepatitis the author discusses, according to Neefe, the two types of this disease. Virus IH hepatitis and SH (homologous serum) hepatitis. IH and SH type of hepatitis are two disease entities, they are caused by specific viruses and they differ epidemiologically, immunologically and clinically. The incubation period of IH hepatitis is 17-34 days, its epidemiologic transmission may be orally and respiratory; whereas in SH hepatitis it is parenterally only. Next the prodromal symptoms of IH hepatitis and the full clinical picture of anorexia, nausea, vomiting, fever, liver enlargement, icterus, are described, also the fact that virus is always found in the stool. The susceptibility to IH of the age-groups below 30, its seasonal occurrence, the factors influencing the severity of a given case and the presence of antibodies to IH in gamma globulin, its

possible prophylactic and therapeutic use are stressed. By means of good community sanitation and through better knowledge of the epidemiology the author believes that further epidemics of IH hepatitis could be prevented.

HANS J. JOSEPH

AN UNUSUAL CASE OF FATAL HEPATIC SARCOIDOSIS: Maurice L. Kelley, Jr. and Robert J. McHardy. Am. J. Med. 18:842 (May), 1955.

Despite the frequent occurrence of hepatic lesions in sarcoidosis, jaundice with fatal hepatic insufficiency is a rare complication. Such a course was observed in a 48-year old white male suffering from progressive obstructive jaundice with hepatosplenomegaly, pruritus and marked elevation of serum bilirubin, alkaline phosphatase and total cholesterol. All flocculation tests were consistently normal. An unusual electrophoretic pattern of the serum protein was present but could be attributed to the high lipid contents. The liver was palpable three fingerbreadths below the umbilicus, it appeared smooth and firm and was slightly tender on pressure, the spleen was equally enlarged. Initial biopsy revealed granulomatous foci while at autopsy one year later severe fibrosis and scarring of the liver was found. The latter changes must be attributed to the prolonged treatment with ACTH, cortisone and x-rays.

H. B. EISENSTADT

CONTRIBUTION TO STUDY OF WILSON'S DISEASE: V. Gilsanz, J. M. Segovia and H. Castro Mendoza, A.M.A. Arch. Int. Med. 95:727 (May), 1955.

Three brothers affected with this disease were examined, one of them was asymptomatic and had aminoaciduria which is characteristic of this disorder and which precedes hepatic and cerebral manifestations by a long time. It must be assumed that the hepatic cirrhosis is due to the prolonged loss of protein in connection with the increased aminoaciduria the latter being caused by a primary familial endogenous fault of the protein metabolism. The excessive mobilization of copper is presumed to be associated with this protein breakdown and is responsible for the cerebral degenerative process because the excessive deposit of this metal in the brain interferes with the respiratory enzymes of the brain tissue. As corticotropin causes a great increase of the aminoaciduria but no increase of the copper elimination and Bal has the opposite excretory effect it must be assumed that both substances are not bound to each other at the time they leave the kidney. It has been shown that the copper is apparently attached to oligopeptides liberated by the same abnormal protein breakdown.

H. B. EISENSTADT

ACUTE CHOLECYSTITIS: Warren H. Cole. Mississippi Valley M. J. 77:85 (May), 1955.

The author feels that acute cholecystitis should be treated surgically if seen within 48 hours of the onset of symptoms providing the diagnosis is obvious. An electrocardiogram should be done to rule out coronary artery disease. Although the incidence of complications may be higher following immediate surgery, the incidence of development of serious complications such as pancreatitis, common duct stone, etc. is less. The author uses smears of the gallbladder content as a guide as to whether the gallbladder should be removed or just drained. If no bacteria are found on smear, the gallbladder should be removed, whereas if numerous bacteria are found, cholecystostomy is his procedure of choice. The most important consideration in the treatment is accurate diagnosis. If there is any doubt, surgery should be held in abeyance.

ABE ALPER

ROLE OF LIVER FUNCTION TESTS AND GENERAL LABORATORY FINDINGS: James L. Borland. J. Florida M.A. 41:926 (May), 1955.

The diagnosis depends upon the natural history of the disease as it develops in the patient; the laboratory tests merely serve as a check upon the reasoning of the physician.

Laboratory tests are guideposts to the clinical logician and as such, are invaluable; but used alone, or blindly, as "liver function tests", they are likely to appear inconsistent and unreliable.

In order to select and interpret the results of any test of liver function, the physician must bear in mind that disease patterns overlap, that the manifestations of the single pathologic process are a summation of various physiologic alterations, that conditions other than those of the liver affect the results, and that although a single substance is being measured, the level in the tissues may be a summation of several different factors. A test may give positive results in the same patient at different times for different reasons.

The tests are unnecessary in most situations, the diagnosis being apparent from the history and physical examination; but as the effect of the disease becomes a more complex algebraic sum, the tests are needed. The factors in this sum usually become so numerous that no single test will fill in sufficient integers for its solution. Multiple tests must be run, usually one from each group, the so-called "liver profile".

BERNARD STERN

THE ROLE OF THE HISTORY AND PHYSICAL EXAMINATION IN THE DIFFERENTIAL DIAGNOSIS OF DISEASES ASSOCIATED WITH JAUNDICE: Eric E. Wollaeger. J. Florida M.A. 41:921 (May), 1955.

Laboratory studies done to help in the differential diagnosis of jaundice, valuable though they may be, must be interpreted in the light of all the information obtainable from a carefully taken history and a meticulous physical examination. A useful classification divides the types of jaundice into three main groups: 1. Hemolytic, 2. Hepatocellular, 3. Obstructive.

Hemolytic jaundice is due to excessive destruction of red blood cells and does not indicate hepatic or biliary tract disease. There is an increase in the indirect reacting bilirubin in the blood. There is no history of the passage of dark urine during attacks of jaundice. This distinguishes it from hepatocellular and obstructive disease in which the jaundice is due to an increase in the blood level of direct reacting bilirubin which is regularly excreted in the urine. Because of the excessive excretion of bilirubin into the biliary tract in hemolytic jaundice, gallstone formation is common (60 per cent of cases). This may lead to obstructive jaundice, so that the two types coexist in the same patient at a given time. The jaundice of constitutional hepatic dysfunction is similar to hemolytic jaundice in that there is an increase in indirect reacting serum bilirubin. This is a benign condition and the patient can be reassured that the jaundice and associated asthenia and fatiguability do not denote chronic hepatic or obstructive disease. Recognition of this entity may enable one to avoid useless or dangerous medical therapy or needless abdominal exploration.

From the practical standpoint, the most important problem in jaundice is to differentiate obstructive from hepatocellular disease. Obstructive jaundice is frequently amenable to surgery whereas patients with hepatocellular damage are not benefited by surgical measures and tolerate them poorly. Pain is seldom an important feature in hepatocellular disease and evidence of disturbance of metabolic function of the liver may be found early, frequently even before jaundice appears. Pain is much more common in obstructive disease. Pain due to a malignant disease is constant and boring, whereas that due to stones is episodic. Symptoms of stricture almost always begin within the immediate postoperative period after the biliary tract has been subjected to surgery.

Mild jaundice is fairly common in portal cirrhosis, but the history of alcoholism, ascites, and hematemesis leads to the correct diagnosis. Pruritus may exist in hepatocellular as well as in obstructive jaundice, although more severe in cases of the latter. Severe itching may occur in various types of cirrhosis. Clay-colored stools do not necessarily denote obstruction as they will be found almost universally in cases of hepatocellular damage as well as among those with obstruction.

Complete and persistent obstruction to the flow of bile is characteristic of carcinoma of the head of the pancreas or common bile duct. Complete obstruction is proved to exist when no bile is obtained by repeated duodenal intubation or by quantitative studies of the feces for urobilinogen. Carcinomatous obstruction to the

bile passages characteristically causes deep and progressive jaundice. An extremely large liver extending well down into the lower abdomen is almost always the site of a malignant process. A palpable distended gallbladder in the abscence of acute cholecystitis denotes the presence of a neoplastic obstruction of the common bile duct below the junction with the cystic duct. Vascular spiders are usually indicative of parenchymatous liver disease and more rarely of long standing obstruction. The presence of edema in the acutely ill patient with jaundice points to serious parenchymal damage.

BERNARD STERN

ROLE OF LIVER BIOPSY: Theodore C. Keller. J. Florida M.A. 41:11 (May), 1955.

The value and limitation of needle biopsy of the liver in the differential diagnosis of jaundice can be presented in four categories: The first concerns its ability to distinguish between obstructive jaundice uncomplicated by infection, viral hepatitis and portal cirrhosis. The biopsy plays its greatest diagnostic role in differentiating between these three conditions. The second concerns a group of conditions which are characterized histologically by obstructive jaundice in conjunction with either acute or chronic pathologic changes of the intrahepatic biliary system. The third concerns its place in the diagnosis of tumors and certain specific infections and the fourth concerns its use as an adjunct in the diagnosis of hemolytic jaundice.

Most needle biopsies are without complications and the mortality and morbidity are minimal. Since bleeding is the most frequent serious complication, biopsy is contraindicated in patients who manifest impaired blood coagulation or bleeding tendencies. Early biopsy is especially important for diagnosis in the jaundiced patient since prolonged obstruction, if unrelieved, inevitably results in either inflammatory or sclerotic changes in the intrahepatic biliary system.

BERNARD STERN

REGURGITATION TYPE OF JAUNDICE DURING PROLONGED THERAPY WITH CHLORPROMAZINE: R. E. Lemire, Jr. and R. A. Mitchell. A.M.A. Arch. Int. Med. 95:840 (June), 1955.

Three cases of obstructive jaundice with marked pruritus were observed during prolonged chlorpromazine therapy for psychotic disorders. They came to an exploratory laparotomy because the jaundice had persisted unchanged for 23 to 25 days. Laboratory findings showed, in addition to hyperbilirubinemia mainly caused by an increase of the direct bilirubin, an elevation of alkaline phosphatase. Total cholesterol was increased only once while cephalin flocculation was always negative. The liver appeared enlarged in one patient but showed no macroscopic abnormalities. Microscopic examination revealed bile plugging of the canaliculi without obstruction of the larger biliary channels. There was an increased cellularity of the portal triads without any important change of the hepatic parenchyma. Similar findings have been noticed after administration of thiouracil, sulfonamides, methyltestosterone, arsphenamine, carbon tetrachloride, and chloroform and are suspected to be not due to hepatic toxicity but to drug hypersensitivity.

H. B. EISENSTADT

LIVER DAMAGE AND EOSINOPHILIA FOLLOWING CHLORPROMAZINE THERAPY: B. S. Hartnett. Brit. M. J. 4928:1458 (18 June), 1955.

This is an interesting and detailed report of jaundice occurring following chlorpromazine therapy and associated with an eosinophilia. Needle biopsy indicated an obstructive type of pathology so that the patient was explored. At the surgical intervention, no evidence of biliary obstruction was noted and no confirmation of an obstructive biliary condition with tube cholangiography likewise was obtained. The patient has been observed for six months following apparent recovery and while the eosinophilia, which at the time of acute illness was 58 per cent, has now become normal, there is still excessive urinary urobilinogen. The question as to whether chlorpromazine can produce permanent liver damage has to be considered in view of this observation.

IRVIN DEUTSCH

BOOK REVIEWS FOR GASTROENTEROLOGISTS

BICKHAM-CALLANDER SURGERY OF THE ALIMENTARY TRACT—VOLUMES I, II AND III: Richard T. Shackelford, M.D., Assistant Professor of Surgery, Johns Hopkins University School of Medicine. Assisted by Hammond J. Dugan, M.D., Assistant in Surgery, Johns Hopkins University School of Medicine. 2,575 pages through Vols. I, II and III with 1,705 illustrations through Vols. I, II and III. W. B. Saunders Co., Philadelphia, Pa., 1955. Price $60.00 per set.

This large text of three volumes has been written and rewritten by the present author. Dr. Shackelford and is one of the most comprehensive texts on gastrointestinal surgery. It is so complete and explanatory that a medical student can readily grasp the technic by studying the step by step illustrations in a given procedure.

Medical students, general practitioners, especially in small localities, doing surgery and all surgeons should make it a "must" to own these indispensable volumes.

INTESTINAL OBSTRUCTION: Owen H. Wangensteen, B.A., M.D., Ph.D., Professor of Surgery, University of Minnesota, Minneapolis, Minn. Third Edition. Charles C. Thomas, Springfield, Ill., 1955. Price $15.00.

The Wangensteen volume on intestinal obstruction, now in its 3rd edition, has been completely rewritten. It contains 364 more pages of text and 79 more illustrations than the previous edition. In these pages, the reader will find discussion of the physiology, pathology and clinical consideration, with emphasis of therapy plus operative procedures. The general surgeon, as well as the general practitioner, will find excellent description of what happens in the abdomen when pathological states occur. How to make a diagnosis, what to do and how to do it, is the theme that the author emphasizes.

It is highly recommended for inclusion in the physician's already overcrowded library.

DIFFERENTIAL DIAGNOSIS—THE INTERPRETATION OF CLINICAL EVIDENCE: A. McGehee Harvey, M.D., Professor of Medicine and Head of the Department of Internal Medicine, The Johns Hopkins University School of Medicine, Physician-in-Chief, The Johns Hopkins Hospital and James Bordley III, M.D., Director, Mary Imogene Bassett Hospital, Cooperstown, N. Y., Clinical Professor of Medicine, Columbia University, New York, Clinical Professor of Medicine, Albany Medical College. 665 pages. W. B. Saunders Co., Philadelphia, Pa., 1955. Price $11.00.

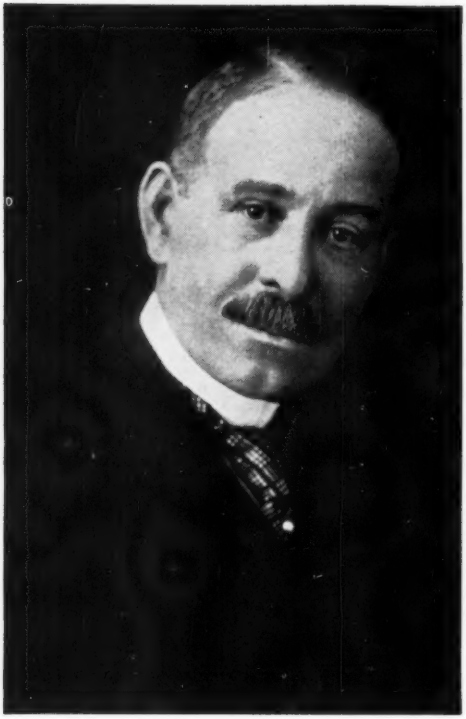
"Differential Diagnosis", although in its first edition, undoubtedly will find a niche in the physician's library. The authors present numerous illustrative cases for diagnostic purpose and give a comprehensive discussion of the history, diagnosis and treatment in the given case. In the unknown cases for study, the physician will recognize some of his own which often defied diagnosis before operation or autopsy.

On page 631, Laboratory Values of Clinical Importance in Adults, will help the doctor in evaluating normal findings and thus aid him to recognize variations when reported by the laboratory of his choice.

This book should be on the desk of practicing physicians.

THE BIOLOGIC EFFECTS OF TOBACCO WITH EMPHASIS ON THE CLINICAL EXPERIMENTAL ASPECTS: Edited by Ernest L. Wynder, M.D., Head, Section on Epidemiology and Associate, Sloan-Kettering Institute of Cancer Research. Foreword by Joseph Garland, M.D., Editor, The New England Journal of Medicine. Little, Brown and Co., Boston, Mass., 1955. Price $4.50.

This is a timely volume, rather complex. It is interesting reading, difficult to assimilate unless one is highly versed in advanced chemistry. The author and his collaborators cover every phase of this controversial question and undoubtedly cigarette manufacturers will be the largest buyers of this book.



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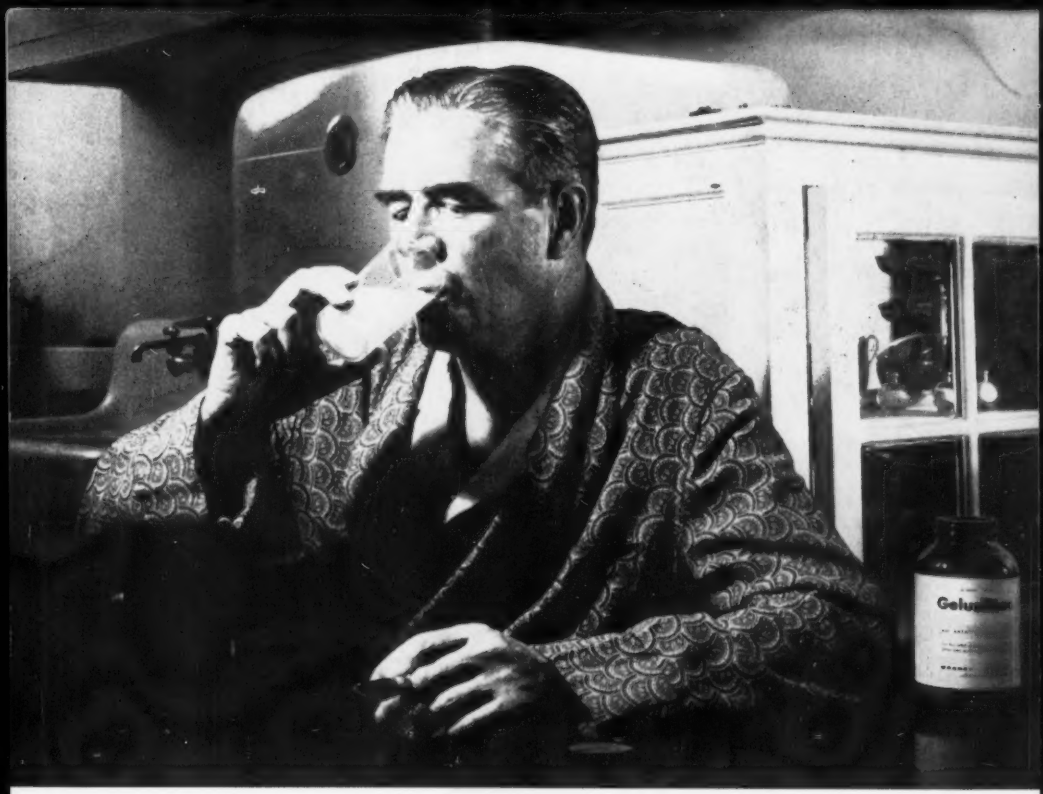

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